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CONGENITAL STENOSIS OF THE ABDOMINAL AORTA*

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STENOSIS and thrombotic obliteration of the descending aorta is a relatively common autopsy finding which is frequently diagnosed during life because there is usually associated a definite clinical picture. Congenital narrowing (with or without occlusion) of the aorta below the isthmus is a rare occurrence, however, and, on account of indefinite symptoms, is seldom diagnosed. This case is recorded because it presents a most unusual picture of narrowing and complete occlusion in the midabdominal aortic segment and extensive compensatory arterial hypertrophy and dilatation. There is added a brief review of the few available recorded cases of stenosis in this region. As the clinical history in this case is also of unusual pathological functional interest, it is included here in greater detail.

CASE HISTORY

M. B., female, aged eighteen years, was first admitted to the Royal Victoria Hospital on June 3, 1929, complaining of palpitation, dyspnea, and precordial pain which resembled pinpricks and radiated occasionally to the left shoulder. These complaints had been present for three months and were aggravated by exertion. She also complained of epigastric distress and nausea without relation to meals for about six months.

Family history was irrelevant.

Personal History.—She gave a history of measles, mumps, diphtheria in childhood, but no history of rheumatic fever. Nocturia (1-2) for past few years. Menses: 13 × 28 × 2 to 3; no dysmenorrhea, menorrhagia, or metrorrhagia. Apart from the diseases mentioned, the patient had always been well and had been able to join in all activities with other children without any difficulty.

Physical Examination.—Temperature was 99.4° F.; respiration, 20; pulse, 95, regular, full volume, high tension. The cheeks were flushed; nutrition, fair. The lungs were normal. The heart extended 9 cm. to the left of the midline at the apex.

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There were an apical systolic murmur conducted to the axilla, and a soft systolic murmur over the base. Both pulmonary and aortic second sounds were accentuated. Blood pressure in arms was systolic, 200 mm. Hg, diastolic, 89 mm. Hg. There was some tenderness in right lower quadrant of abdomen. Urine was negative. Red blood cells numbered 3,880,000; white blood cells, 10,000; hemoglobin, 75 per cent. Electrocardiogram showed slight right-sided preponderance. Blood Wassermann reaction was negative. X-ray films of the arms and legs showed no calcification of the arteries. Special examinations of the eyes, ears, nose, and throat revealed no abnormalities. The clinical diagnosis was essential hypertension.

She was discharged on July 13, 1929, little improved, and attended regularly at the Medical Out-Patient's Department until her second admission to the wards on March 16, 1932.

During this period it was found that the blood pressure in the arms remained as before, while in the legs it was definitely lower, the systolic pressure being about 130 mm. Hg, and the diastolic about 110 mm. Hg. Sometimes the pressures could not be read in the legs. Sometimes the pulse could be detected only in the femoral arteries (usually better in the left one), while at other times it was palpable in both femoral, popliteal, posterior tibial, and dorsalis pedis arteries. There was no edema of the lower limbs, but they were occasionally colder than normal. There was persistent tachycardia (120), and the heart was enlarged to the right and left. A harsh systolic murmur was heard at the tricuspid area and at the base, which murmur was conducted out to the left axilla and up into the arteries of the neck; it was also audible posteriorly at the inferior angle of the left scapula and on each side of the spine from the tenth thoracic vertebra to the midlumbar region, becoming fainter in the lower part of this area. She complained of dyspnea on exertion, palpitation, and occasional indefinite precordial pain radiating to the left arm and the upper part of the back. On several occasions during this period she complained of alternating diarrhea and constipation; blood was found in the stools. Her weight fluctuated between 85 and 95 pounds. Her general health was poor, and she slept badly. The clinical diagnosis was coarctation of the aorta.

The patient was readmitted on March 16, 1932, complaining of palpitation, dyspnea and choking sensations, precordial pain radiating to the left arm, pain in the back over the fifth to the tenth thoracic vertebrae, headache, weakness, nocturia, sore throat with pain beneath the sternum on swallowing, and loss of 3½ pounds in three weeks. The precordial pain and pain in the back had been present for three weeks, the sore throat and dysphagia for one week, while the other complaints had been present periodically since her first admission.

Physical Examination.—Temperature was 100° F.; pulse, 130; respiration, 22. A thin, pale, asthenic, nervous patient, with marked pulsation of the left side of the chest. There was slight infection of the left middle turbinate, and congestion of the nasal mucosa. The teeth were carious. The chest was thin and narrow with prominent ribs; the expansion was good and equal; no abnormalities were found in the lungs.

Cardiovascular System.—There was a pronounced pulsation of the left side of the chest. The pulse was regular, collapsing; the volume, moderate; and the tension, greatly increased. The carotid and brachial arteries pulsated strongly. No pulsation was felt over the abdominal aorta or femoral arteries, but a pulse was detected in both dorsalis pedis arteries. A capillary pulse was observed in the nail beds and lips. Blood pressure in the right and left arms was systolic, 210, diastolic, 60; right leg—systolic, 118, diastolic, not obtained (measured in dorsalis pedis artery).

The apex beat was sharp, the point of maximum impulse being in the fifth left interspace, 9.5 cm. from the midline. The left border of the heart reached to the axilla. The sounds were loud and clearly audible. At the apex the first sound was increased and accompanied by a systolic murmur; the second sound was loud and

harsh. A systolic murmur was heard over the right border of the sternum, being loudest at the level of the xiphisternum, where the tortuous internal mammary artery could be palpated. This murmur was propagated along the seventh, eighth, and ninth right intercostal spaces; it continued downward over the abdomen to the umbilicus where it branched and was lost. A similar softer systolic murmur was audible over the left sternal border, but the left internal mammary was not palpable; this murmur could also be traced along the seventh, eighth and ninth left intercostal spaces. At the base the second aortic sound was ringing and accentuated. Posteriorly a harsh systolic murmur was heard over the fifth to the tenth thoracic vertebrae, and along the twelfth rib, and at the inferior angle of each scapula. There was some tenderness over the fifth to tenth thoracic vertebrae and over their attached ribs.

The fundi showed arterial pulsation. The electrocardiogram was normal. Blood Wassermann reaction was negative. Red blood cells numbered 3,880,000; white blood cells, 11,350 (two hours after eating); hemoglobin, 55 per cent (Sahli). The urine was normal. Blood culture was negative.

A collateral circulation was thought at this time to exist and to be as follows: (1) Between the seventh, eighth, and ninth intercostal arteries and the internal mammary arteries (indicated by the systolic murmurs and palpable right internal mammary artery); (2) between the internal mammary and the epigastric arteries (not conclusively demonstrated, thought to be hidden by recti muscles); (3) between the subscapular and intercostal arteries, as indicated by the systolic murmurs at the inferior angles of the scapulae.

X-ray examination of the chest showed an enlarged heart with a widened aortic arch. The left border of the descending aorta could be followed to the diaphragm; on each side of the vertebrae was a white line, extending on the left from the fifth to the twelfth thoracic vertebrae. It was thought that the right-hand line might be due to ligaments, while that on the left was considered most unusual. Focusing on the ribs with the Bucky diaphragm showed no erosion and suggested a constriction of the aorta just above the diaphragm.

The patient was discharged on April 3, 1932, with some improvement in the rhinitis, but otherwise unchanged. She attended the out-patient department until April 24, 1933. During this period a visible pulsation was seen in the left superior epigastric artery and in the region of the right supraspinatus muscle. She then developed periodic attacks of diarrhea and crampy abdominal pains for which she was again admitted to hospital on April 24, 1933.

Physical Examination.—Temperature was 99.8° F.; pulse, 112; respiration, 22. She was fairly well nourished, alert, and cooperative.

Cardiovascular System.—Slight cyanosis of the fingers, but no clubbing, was noted. A capillary pulse was detected, and the radial pulse was collapsing in character. A slight pulsation was felt in the femoral arteries but none in the popliteal, dorsalis pedis, or posterior tibial arteries. A visible arterial pulsation was seen in the epigastrium, and a large artery was palpable at the inferior angle of each scapula. No visible or palpable arterial pulsation was seen in the supraspinous area.

Blood pressure in the right arm was systolic, 215; diastolic, 70; in the left arm systolic, 204; diastolic, 70.

The apex beat was palpable in the left fifth interspace, 9.5 cm. from the midline and was strong and forcible. There was a questionable apical presystolic thrill, a short fine systolic thrill over the pulmonary area, and a soft systolic thrill over the carotid arteries. The closure of the pulmonary valves was distinctly felt.

The relative cardiac dullness measured 7 cm. at the second rib, 3.5 cm. to the right of the midline, and 9.5 cm. to the left of the midline, in the fifth interspace. The sounds were clearly audible, the pulmonary second sound being accentuated. A loud systolic murmur preceded by a short presystolic murmur was heard over the xiphoid process, the systolic element being propagated up the sternum with diminishing intensity and into the left axilla, and less so to the right of the sternum. Posteriorly on both sides of the spine a systolic murmur was heard faintly from the second to the fourth thoracic spines, more loudly from the fourth to the tenth thoracic spines, and quite loudly from here to the base of the spine. The second sound was accentuated in this area. The electrocardiogram showed a slurring of the QRS complex in all three leads and large T-waves, with abrupt take-offs in Leads II and III.

Cysts of *Endameba histolytica* and *Chilomastix mesnili* were found in the stools.

Blood examination revealed red blood cells, 3,950,000; white blood cells, 10,000; hemoglobin, 75 per cent. The blood Wassermann reaction was negative. The blood Kahn reaction was one-plus.

Courses of emetine were administered, and the patient was discharged on June 6 with improvement in her diarrhea and with disappearance of animal parasites from the stools, but her circulatory condition was unchanged.

Her out-patient record until Nov. 9, 1933, records frequent complaints of diarrhea and the presence of *Endameba histolytica* and *Chilomastix mesnili* in small numbers in the feces. Occasionally the patient complained of weakness of the legs.

She was readmitted on Nov. 9, 1933, with complaints of watery stools with occasional blood for five months, pain on defecation, dysuria and pruritis ani for two weeks, and complaints referable to the circulatory system, similar to those on the previous admissions. In addition, she stated that her feet were continually cold and that she had crampy pains around the knees after walking. She denied any edema of the feet or legs. Her general health for the past two months had been poor.

Physical Examination.—Temperature was 99.4° F.; pulse, 80 (Nov. 9, 1933). She was a poorly nourished, asthenic, nervous female with a marked malar flush.

A capillary pulse was noted in the lips and nail beds. The radial pulse was collapsing, and accentuated pulsation was seen in the brachial and carotid arteries. A weak pulsation was felt in the abdominal aorta and the femoral, dorsalis pedis and posterior tibial arteries. The blood pressure in the arms was systolic, 225; diastolic, 40; left leg, systolic, 80; diastolic, not obtained. The whole precordium exhibited a marked pulsation. A systolic thrill was palpable at the base and in the upper seven intercostal spaces pulsating vessels could be felt.

The apex beat was situated 12 cm. to the left of the midline. The sounds were loud in all areas. At the apex a systolic murmur was heard, and the second sound was harsh and accentuated. A harsh systolic murmur was audible over the pulmonary area and over the fifth thoracic spine.

There was generalized tenderness over the abdomen. The legs and feet were cold. Motile and encysted amebas were found in the stools, together with mucus and blood and occasionally pus. The blood Wassermann reaction was negative. The blood culture was negative. The x-ray film of the chest showed the heart to be enlarged, with accentuated shadows of the great cervical vessels. There was slight irregularity along the lower borders of the ribs. Blood examination revealed red blood cells, 4,380,000; white blood cells, 14,200; hemoglobin, 80 per cent.

In spite of treatment with emetine and carbazone, the patient lost weight, and the diarrhea failed to improve. On January 11, there was an exacerbation of the intestinal condition. The temperature rose to 102° to 104° F., and the pulse to about 140; the frequency of the stools became greater with larger quantities of gross blood.

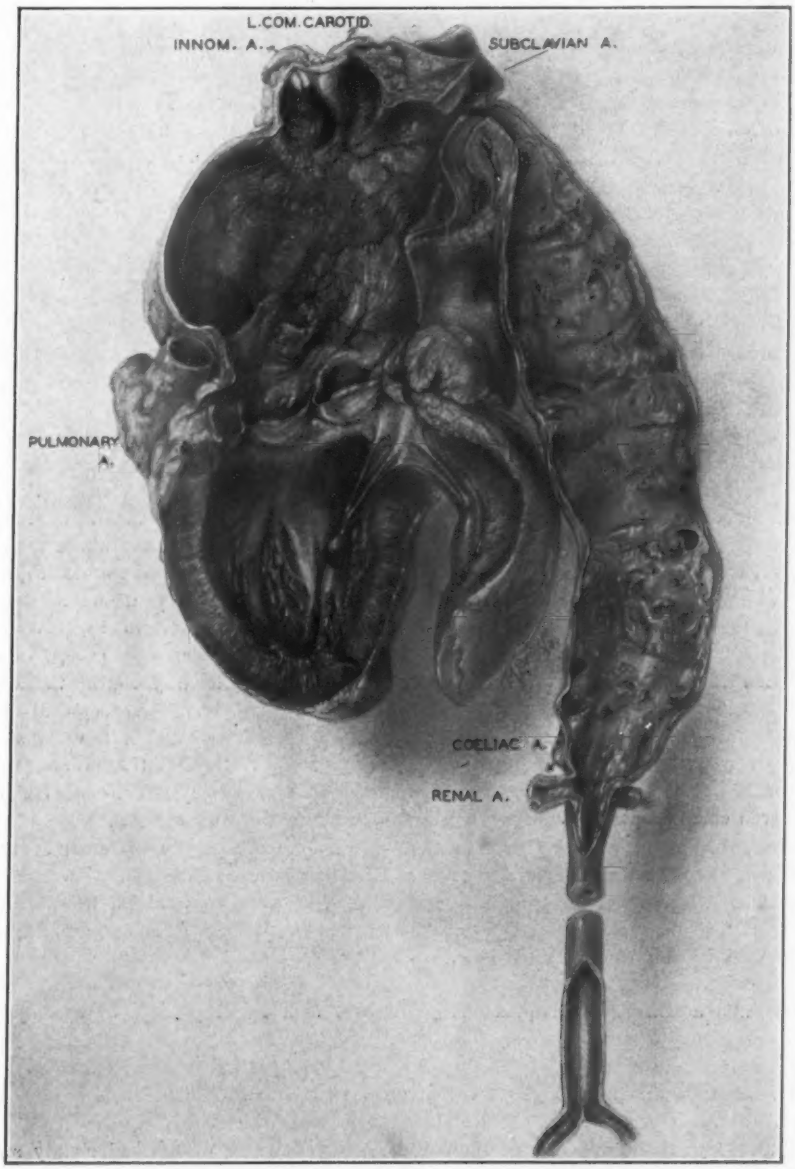

Fig. 1.—Congenital stenosis of midabdominal aorta.

On January 13 the red blood cells numbered 4,034,000; white blood cells, 15,500; hemoglobin was 48 per cent. On January 25 she was transferred to the surgical side for the performance of an ileostomy. At operation it was found that the cecum had ruptured, and an abscess had formed. The abdomen was drained through a gridiron

incision, but the patient gradually failed. The temperature was intermittent, the pulse 150, and she passed numerous watery stools and suffered severe abdominal pain. She sometimes vomited feculent material. She died on Jan. 30, 1934, three days after operation.

SUMMARY OF AUTOPSY FINDINGS

Gross Examination (eighteen hours after death).—The body was small and poorly nourished, 150 cm. long. The abdomen was rounded and tense and showed a linear incision 12 cm. long in the right lower quadrant through which protruded two rubber drains.

The thoracic viscera appeared in normal relation to each other, and the lungs were slightly emphysematous. The right heart was slightly dilated with chicken-fat and cruor clot, and the left ventricle was firmly contracted. There was slight thickening of the left ventricular wall including its papillary muscles. There was no valvular lesion, however, except some irregular thickening at the free margin of aortic cusps. Both ductus arteriosus and foramen ovale were closed. The organ weighed 360 gm. after having been opened.

Aorta.—Three centimeters above the valve, the ascending portion bulged to the right, forming a saccular aneurysm, 8.5 cm. at its greatest circumference. This ended at the beginning of the transverse arch where the circumference was 5.5 cm. There was a calcified plaque at the isthmus but no definite narrowing at this level; 1.5 cm. below the renal branches, however, there was an abrupt diminution in size, with the formation of a firm cord 3 cm. long and about 8 mm. in diameter. The lumen here was completely occluded by a firm gray laminated mass which fused with the vessel wall. It became patent again 4.5 cm. above the bifurcation where the circumference was 1.5 cm. In marked contrast to the gross changes in the aorta proximal to the stenosis, the portion below the occlusion and the iliac branches were very delicate and well preserved. These changes are well illustrated in Fig. 1. The proximal aorta showed a marked uniform thickening to about 5 mm. except in the stretched aneurysmal sac where a firmly attached, reddish gray mural thrombus filled its deeper parts. The intima of the ascending and transverse segments had many linear puckerings, mostly parallel to the long axis of the vessel, between which were smooth, slightly elevated, gray and yellow patches. Beyond the isthmus these puckerings disappeared while the yellow patches became more numerous between scattered calcified plaques and small irregular atheromatous ulcerations.

The inferior mesenteric and ovarian arteries were completely occluded at their origin in the thrombosed aortic segment. Branches of the celiac axis as well as innominate, left common carotid, and left subclavian arteries were thick-walled and dilated. The internal mammary arteries were widely dilated, thickened, and slightly tortuous, especially on the right side.

The abdominal cavity contained coils of bowel dilated with gas and fluid feces. There was a diffuse fibrinopurulent peritonitis with small pockets of creamy pus between loosely adherent loops. This peritonitis was apparently an extension from a perforated ulcer in the cecum. There were multiple irregular undermined deep and superficial ulcers throughout the colon having the characteristic appearance of amebic dysentery infection. The left kidney contained a well-organized infarct, and all parenchymatous organs showed the gross features of marked cloudy swelling. The intracranial contents were not examined.

Microscopic Examination.—For the purpose of this report, the description will be confined to pathological changes in the circulatory system.

Aorta: Sections from various parts proximal to occlusion showed quite a similar picture. There was marked irregular swelling (increase) and fusion of the intima with poorly defined fragmented internal elastic lamina. The adjacent inner half of

the media contained markedly swollen and fused fibers between patches of typical atheroma. This did not take the van Gieson stain. Elastic fibrils were here also

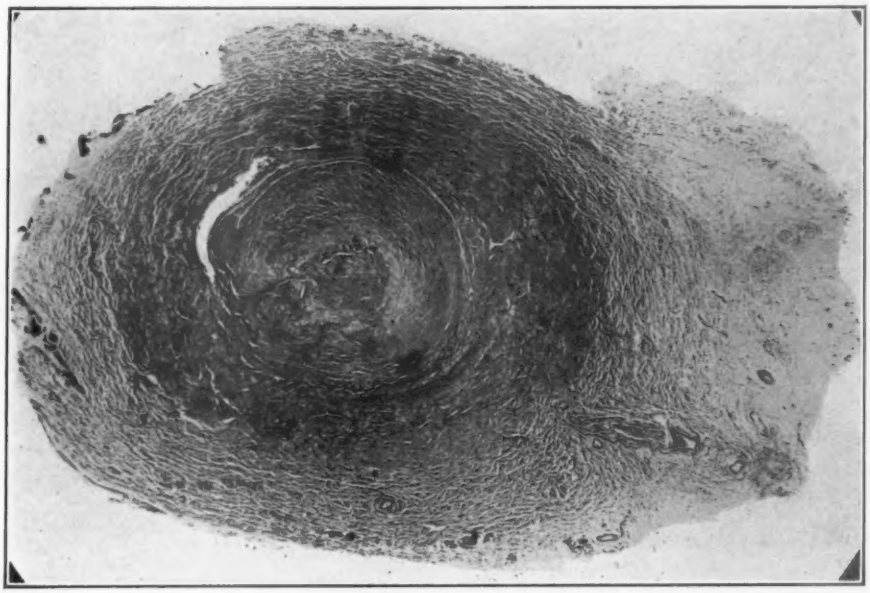

Fig. 2.—Transverse section of stenosed segment of abdominal aorta. There is complete fusion of the coats and dense hyaline fusion of the inner half of the wall. Organized laminated clot with limited recanalization fills the small lumen. (×20.)

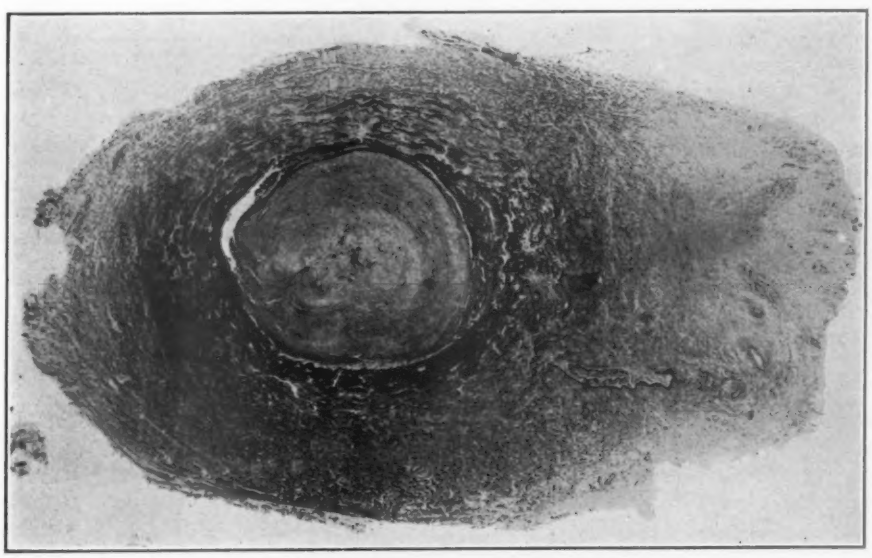

Fig. 3.—Orcein-van Gieson preparation of same section as Fig. 2. Increased fragmented elastic fibrils stain black, and collagen appears dark gray. (×20.)

abundant and extensively fragmented. The adventitia showed marked increase in fibrous tissue, throughout which were many vasa vasorum having uniformly thickened walls. Some were surrounded by small round cells which extended throughout

Fig. 4.—Descending thoracic aortic wall. Some of the thick vasa vasorum are surrounded by small round cells. There is marked gelatinous swelling and hyaline fusion of inner half of media. (×35.)

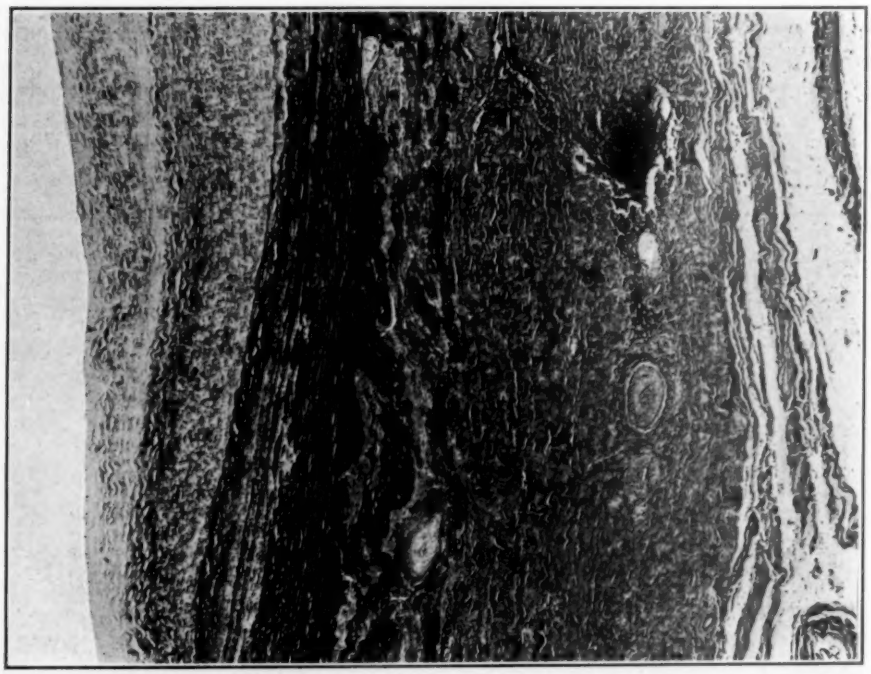

Fig. 5.—Orcein-van Gieson preparation of same section as Fig. 4, showing condensation and marked fragmentation of abundant elastic lamellae. (×35.)

the adjacent outer half of the aortic media, but there was no definite fibrous tissue scarring. There was no definite endarteritis of the vasa vasorum. The thick adventitia also contained many large medullated nerves. In the sections from the aneurysmal dilatation there was an irregular mass of fibrin which fused with the adjacent intima by scattered proliferating fibroblasts. In places this recent thrombus fused with a deeper zone of more mature fibrous connective tissue. Except for stretching of the coats and extreme fragmentation of elastic fibrils, the histological picture was similar to that of other parts. Immediately above the occluded segment the intimal and medial thickening and hyaline fusion became more extensive. In the media, only small fragments of muscle fibers and elastic fibrils remained, while well-preserved dense fibrous tissue persisted in the adventitia.

At the area of occlusion the lumen was completely filled with a homogeneous, pale red, hyaline mass, with a few small recanalized endothelial spaces containing scattered red blood cells. At the periphery this mass fused with dense fibrous tissue having small nuclei and abundant fibrils. This fibrous connective tissue extended throughout the fused aortic coats with variable degree of hyaline fusion. Orcein and Weigert's elastic tissue stains showed extensive fragmentation of elastic fibrils throughout the inner half of the vessel, while the outer half contained small arteries (vasa vasorum) having thickened mediae. There was no conclusive evidence of a syphilitic process. Below the occluded area and in the iliac arteries all coats were very well preserved.

DISCUSSION

This is apparently a case of *congenital stenosis* of the lower part of the abdominal aorta with subsequent thrombosis and recanalization. This opinion is arrived at, however, only after inflammatory and regressive lesions have been carefully considered and excluded. The distribution of hypertrophy and arteriosclerosis in this aorta is important anatomical evidence of a long-continued stenosis. These changes are entirely proximal to the obstruction and indicate a prolonged hypertension. Thus the hypertrophy of these coats is compensatory to a prolonged high aortic pressure. On the other hand, the lower segment and common iliacs below the stenosis (where there was a diminished pressure effect) remain extremely delicate and well preserved. To produce such an anatomical picture, we must assume a marked obstruction to blood movement (due to the narrowed lumen) for years before thrombosis occurred. It is well recognized that advanced atheroma may be associated with complete thrombus formation, but this is nearly always confined to muscular arteries. In the aorta, pedunculated mural thrombi, which only partly occlude the lumen, are far more common unless retrograde extension from adjacent branches has occurred. An isolated complete thrombus in this segment of the aorta suggests that there was a predisposition because of an unusually narrow lumen. The dense scar tissue throughout the fused coats, in the histological sections, adds further support to this opinion.

It is perhaps more difficult to exclude syphilis as the primary causal factor for the aortic lesions above the obstruction. Aneurysmal dilatations due to syphilis are, of course, extremely common, and stenosis

has also been described. The histological picture, however, is not typical of a specific inflammation. The absence of medial scarring and of endarteritis of the vasa vasorum is noteworthy. There was no familial or personal history of syphilis, no clinical signs, and the serological reactions were negative. Gsell[9] and later Erdheim[7, 8] have described cases of hypertension with aneurysms in the ascending aorta which were associated with diffuse medial gelatinous swelling and sometimes cystic degeneration. Since their observations at least fourteen similar cases have been reported, all having negative serum Wassermann reactions and no clinical or anatomical evidence of syphilis. Such a case has recently been observed at this Institute.[4] The constant dilatation of the ascending aorta may be partly attributed to a purely mechanical effect. This is its greatest diameter and therefore is the situation of greatest expansive pressure (Oppenheim).[17] It is the favored situation for permanent dilatation of the aortic wall. Although the histological picture in this case is not that of diffuse aortic medial necrosis, the extreme patchy intimal and medial degeneration (associated with prolonged hypertension) must be considered the important factor in the aneurysmal dilatation.

The hypertrophy and the dilatation of arteries concerned with collateral circulation are the final and conclusive evidence of the long duration of the stenosis. This was most marked in the intercostal and internal mammary arteries. Although the inferior mesenteric and ovarian branches could not be differentiated in the stenosed segment, there was no infarction of the colon or ovaries. This indicates that sufficient collateral circulation had been slowly established to these tissues to allow maintenance of function. Adequate circulation to the lower extremities was provided through anastomoses with the superior and inferior epigastric arteries.

It is impossible to do more than assume any relation between the thrombus in the aneurysm and that in the stenosed aortic segment because both vary greatly in age in different locations. If the thrombus at the site of stenosis was formed about an embolus, we must still assume a slowly progressive block in order to explain the absence of infarcts and the presence of marked compensatory hypertrophy and dilatation of those arteries concerned with collateral circulation.

Reference has already been made to syphilitic stenosis of the aorta. This is extremely rare. Hickl[12] found only two recorded cases up to 1931, and these were described by Stadler[20] as limited constrictions at the isthmus less than 1 cm. in diameter. Nonspecific mesaortitis may produce a constriction, but instead of an extreme abrupt stenosis there usually occurs a long funnel-shaped narrowing of the lumen, as demonstrated in Hickl's case of diffuse mesaortitis following rheumatic fever.

It has been noted that congenital stenosis at the aortic isthmus (coarctation) is quite frequent and this subject has been extensively reviewed by Abbott.[1] On the other hand, congenital stenosis of the aorta below the insertion of the ductus arteriosus has been rarely described during the past century. The first case was apparently reported by Schlesinger[22] in 1835. It concerned a girl aged fifteen years who had severe dyspneic attacks accompanied by tonic and clonic convulsions for two years. The thoracic aorta was almost completely obliterated to a thin cord for two inches above the diaphragm so that a fine sound could be passed through it only with difficulty. Above the stenosis the aorta was widely dilated and gave rise to many abnormal branches; the internal mammary and subclavian arteries were also much enlarged.

Duncan,[6] describing a case of thrombosis of the abdominal aorta in 1843, writes "many cases are now on record in which the aorta has been found obliterated, some of them at the same point as in this specimen, some with gangrene, others not. Many of these have evidently been congenital. . . ." He gives no references. Power[18] in 1861, described a youth aged seventeen years, who suffered from palpitation and epileptiform attacks following a "fever" and exhibited marked pulsation of the carotid, temporal and subclavian, internal mammary, and epigastric arteries. At autopsy there was found stenosis of the aortic valve and hypertrophy of the left heart. The internal mammary and epigastric arteries were dilated and very tortuous, and the aortic arch was enlarged. The abdominal aorta, after giving off its visceral branches, was found greatly diminished in size, and the iliac branches were correspondingly small. Power refers to the stenosis of the abdominal aorta as "an arrest of development" but does not discuss it further. Barié[2] states that Kriegk could find no other cases of congenital aortic stenosis below the isthmus prior to 1878, but couples Schlesinger's name with that of P. L. A. Nicod, who apparently described an analogous case in 1818. Bonnet[3] states that there were no similar cases reported between 1878 and 1903.

In 1911, Hasler[10] reported the findings in a man who had always been in good health till he died of lobar pneumonia at the age of forty-nine years. The heart was slightly dilated and greatly hypertrophied. Just above the aortic valve the aortic circumference was 7 cm.; distal to the origin of the left subclavian it narrowed, rather abruptly, to 3.5 cm., and then widened to 4.5 cm. in circumference. At 3 cm. above the diaphragm it suddenly became completely obliterated to form an impervious fibrous cord, 7 mm. in diameter and 2.5 cm. long. There was a well-developed collateral circulation through the intercostal, internal mammary, and epigastric arteries. Hasler believed that this stenosis was due to some acquired disease, whether intrauterine or postnatal, but could find no evidence on

histological examination of scar tissue, newgrowth or syphilis, and concluded that the narrowing was the result of an autochthonous organized thrombus of unknown origin.

Costa[5] in 1930 described the case of a female, aged forty-nine years, who died suddenly in the street. At autopsy there was found a rupture of the first left intercostal artery and extensive hemorrhage into the mediastinum and prevertebral connective tissue. Between the first and second pairs of intercostal arteries a pronounced annular constriction of the aorta was found. The aortic coats above and below this stenosed area appeared grossly normal, and the caliber of the proximal part of the aorta was not larger than usual. On histological examination the intima proximal to the stenosis was thickened and fibrous but showed no degenerative changes. The other coats were essentially normal. At the site of narrowing, however, the intima and the inner half of the media appeared to be separated and partly invaginated, thus encroaching on the lumen to form a narrow diaphragm. The outer half of the media and adventitia at the level were slightly indented. Below this stenosis the intima, extending into the iliac and femoral arteries, was thickened and fibrous. In the muscular arteries there was an increase of fibrous tissue throughout the media with patchy fatty degeneration and calcification. Costa suggests that the aorta had maintained its embryonic caliber due to the presence in its wall of residual tissue from the primitive right aorta which normally joins the left one at about this level.

The most recently reported case is by Schleckat[21] in 1933. A man, forty-four years old, complained of a feeling of fullness and pressure in the chest, occasional eructation of gas, poor appetite, and distressing thirst for four years. He died of bronchopneumonia. There was found at autopsy a constriction in the aorta at the level of the diaphragm which just admitted a 3 mm. probe. The aorta above the narrowed part was uniformly dilated, and the heart was described as "three times the size of the fist." Below the stenosis the aorta was of normal size. Throughout its length, the intima showed many atheromatous plaques. Microscopically there was a patchy diffuse and circumscribed thickening of the intima with deposits of "lipoid." The media was everywhere intact, and the adventitia showed focal collections of small round cells, which did not penetrate the media. The serum Wassermann reaction was three-plus; the Meinecke test was negative. Schleckat believes, like Costa, that the stricture was due to some irregularity in the development of the system of aortic arches.

It is impossible to state exactly the causal mechanism of the stenosis of the abdominal aorta in the case reported here. None of the authorities consulted (Herxheimer,[11] Hochstetter[13] Keibel and Mall,[14] Keith,[15] von Kölliker,[16] Rückert and Mollier[19]) mention such an

anomaly, and any explanation can only be hypothetical. It is known that the two dorsal aortas (omphalomesenterics) are partly fused in the human embryo of 23 paired somites, i.e., about the fourth week of fetal life (Thompson[23]). Shortly after this they fuse completely, forming a single blood channel. Faulty fusion is known in rare cases to result in an aorta which is divided longitudinally into two by a thin partition (von Kölliker). It is therefore possible that stenosis of the abdominal aorta, as found in this instance, was due to (1) lack of, or unequal fusion of, the two dorsal aortas at one point with obliteration and loss of one of them; (2) kinking of the fused aortas with consequent localized increased longitudinal tension producing a permanent narrowing. Of these it would seem that the first is the more probable and thus fits into the general category of developmental inhibitory faults which result from imperfect, or lack of proper, fusion of originally dual embryonic parts with reduction or loss of one of them. The exact causes of this inhibition remain obscure. No evidence was discovered which would make it likely that this lesion resulted from an acquired intrauterine disease.

SUMMARY

An unusual instance of congenital narrowing and complete occlusion of the midabdominal segment of the aorta, immediately below the renal branches, in a woman aged eighteen years, is described. The case was clinically under observation for nearly five years, and the circulatory changes and the collateral circulation were followed and studied. During the last year of her life she developed an infection of amebic dysentery to which she succumbed, in spite of active treatment, with a perforated cecal abscess.

Autopsy disclosed the midaortic narrowing and thrombotic obstruction with a tremendous aortic widening above it. Below it the aorta and the iliac branches were delicate and well preserved. The collaterals were prominent and thick walled. A careful anatomical study of the case led to the conclusion of a congenital anomaly from lack of proper fusion of the original two dorsal aortas, with regression and loss of one of them. This, judging from the literature and the number of reported cases, which are briefly reviewed, must be an extremely rare occurrence.

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HEMODYNAMIC STUDIES IN EXPERIMENTAL CORONARY OCCLUSION*

I. Open Chest Experiments

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FOLLOWING acute occlusion of a main coronary branch in the human or in an experimental animal there occur a series of events which lead to death in a high percentage of the cases. Although it is generally recognized that death under these conditions is attributable to changes in the circulation as a whole as well as to local changes within the heart, there are available relatively few objective contributions to the hemodynamics of the circulation as a whole following acute coronary branch occlusion. This is largely due to the fact that until recently there were no accurate means for studying the various factors which reflect the status of the entire circulatory system.

In recent years, however, several important contributions have been made in this field. Orias[1] ligated the anterior descending branch of the left coronary artery in dogs and noted the effects on the circulation by means of strategically placed sensitive manometers. The contractions of the left ventricle immediately became markedly hypodynamic. There was a similar but less marked effect on the right ventricle. Although the cardiac output was not measured as such, Orias believed that it was probably profoundly diminished. In many of his cases the pressure rose within several minutes to normal or above normal. Orias concluded that in these cases the ventricle reacted to the increased stretch. He did not take into account the possibility that the output might still be reduced, the normal or elevated pressure being due to a compensatory peripheral vasoconstriction.

Fishberg, Hitzig and King[2] studied the hemodynamic effects of coronary occlusion in man and believed the shock to be probably "peripheral." They measured the blood volume in twenty-nine of their cases and interpreted their results as indicating a tendency toward diminution. Study of these cases reveals only one in which the blood volume was unequivocally subnormal. What collateral factors were present in this case, or whether an error in technic could have been made, is conjectural.

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On clinical grounds, T. R. Harrison[3] states: "Aside from the pain, the most striking clinical phenomena in persons with coronary thrombosis are those referable to the acute alterations in the dynamics of the circulation. These phenomena are of two types: one group, such as weakness, dizziness, faintness, syncope, unconsciousness, feeble heart sounds, diminution in blood pressure and especially the pulse pressure, alternation and feebleness of the pulse, pallor, dusky cyanosis, and subnormal temperature being due to diminished cardiac output because of sudden damage to the heart. The second group of circulatory phenomena are those of congestive heart failure dependent on acute dilatation of heart."

The present report* deals with an investigation on the hemodynamics of the circulation in dogs following sudden ligation of the left anterior descending branch 2 cm. below the left coronary ostium. Inasmuch as the numerous experimental procedures produce considerable pain, all studies were carried out with the animals under anesthesia. We confined our control studies to (a) the effect of anesthesia alone and (b) the effect of anesthesia followed by thoracotomy and coronary artery dissection without ligation. In the latter series, as well as in the coronary ligation group, the tests were made after closing the chest. The changes which will be described are to be considered only in relation to the conditions under which the experiments were carried out. In order to eliminate the immediate effects of thoracotomy, similar studies were carried out in ten additional dogs following left anterior descending branch ligation in the closed chest. This was accomplished by a special procedure which, together with the results obtained, will form the subject of a separate communication.

With the object of obtaining a relatively complete picture of the circulatory changes which follow these procedures, the following factors were investigated in thirty dogs (10 dogs in each group):

1. Cardiac output.
   (a) Minute volume; (b) stroke volume.
2. Circulation time.
   (a) Ether method; (b) cyanide method.
3. Arterial blood pressure.
4. Venous blood pressure.
5. Blood volume.
   (a) Cell volume; (b) plasma volume; (c) total volume.
6. Serum proteins.
   (a) Albumin; (b) globulin; (c) total.
7. Hemoglobin per cent and erythrocyte count.
8. Temperature.

*For a preliminary report of these findings see Proc. Soc. Exper. Biol. & Med. 33: 446, 1936.

METHODS

Suitable methods for carrying out the numerous tests rapidly and efficiently were developed in a series of preliminary experiments. It may be of value, therefore, to describe the procedures in their proper order. The dog, usually weighing from 10 to 20 kg., was not fed for twenty-four hours. The animal was strapped on its back to an operating table, the straps holding down the four paws and upper teeth. Enough nembutal (pentobarbital sodium) was given via an ear vein to produce satisfactory anesthesia. Between 5 and 10 grains were usually needed, i.e., ½ grain per kilogram of body weight. A tracheal catheter was inserted and oxygen consumption measured by the method to be described. The femoral artery was then punctured and the mean arterial blood pressure measured. Five cubic centimeters of blood was withdrawn from the other femoral artery for arterial blood oxygen determination. Then the right heart was punctured to obtain 5 c.c. of mixed venous blood for oxygen determination. The first blood volume sample was withdrawn from the right external jugular vein. With the needle in place, the venous pressure was measured with an L-tube (observing the precautions to be described), following which 5 c.c. of Congo red dye solution was injected. Five minutes later the second blood volume sample was withdrawn from the left external jugular vein. Again leaving the needle in place, ether was injected and the ether time measured. Several minutes later, cyanide solution was injected for the cyanide time. The temperature was taken per rectum, and the dog weighed. The hemoglobin, erythrocyte, and serum protein determinations were done from the first blood volume sample. For any one series of experiments, usually carried out in from 20 to 30 minutes, about 30 c.c. of blood in all were withdrawn.

The cardiac output* was determined by means of the Fick principle,[4] viz.:

$$\text{Minute volume} = \frac{\text{oxygen consumption per minute}}{\text{volume \% arterial blood oxygen} - \text{volume \% mixed venous blood oxygen}} \times 100;$$

$$\text{Stroke volume} = \frac{\text{minute volume}}{\text{heart rate}}.$$

The oxygen consumption was measured with a 1935 Sanborn basal metabolism apparatus. It was attached to a tracheal catheter at the end of which a rubber cuff was inflated to prevent leakage. As an additional precaution, the throat and mouth were packed with wet gauze. The slope of the kymographic tracing was usually quite straight, and a leak was very easily detected. While the oxygen consumption was being measured, the pulse rate was determined twice. The arterial blood was collected in an oiled syringe by puncturing a femoral artery. The blood was then quickly introduced under oil into a test tube, the bottom of which had been coated with enough oxalate to make a 0.3 per cent solution. It was then kept on ice until the determination was made. The venous blood was obtained with a lumbar puncture needle. If the needle was inserted in the third interspace to the right of the sternum pointing posteriorly, inferiorly, and only slightly mesially, the right ventricle was usually punctured with ease. The color of the blood and the pressure in the syringe were usually good indices of whether the needle was in the right or left ventricle. If there was any doubt, another sample was obtained. This mixed venous blood was treated like the arterial sample. The oxygen determinations were made within a few hours by the Van Slyke method,[5] each determination being checked within a fraction of a millimeter of mercury. These procedures were found to be of sufficient refinement for our purposes.

*Our results (Tables I, II and III) are tabulated in the traditional manner. The cardiac output refers only to that of one ventricle. To estimate the total output, the volume is multiplied by 2.

The blood volume was measured by a modification of the Keith, Rowntree and Geraghty[6] dye injection method. This unpublished modification was introduced at the Mount Sinai Hospital by Dr. Nathan Rosenthal. Two large drops of 20 per cent potassium oxalate solution were put into two graduated 15 c.c. centrifuge tubes. Ten cubic centimeters of blood was withdrawn from the external jugular vein, avoiding mechanical passive congestion. The blood was run slowly down the sides of the centrifuge tube to prevent the formation of bubbles, and was then mixed with the oxalate solution by inverting the tube several times. Five minutes after the injection of 5 c.c. of 1 per cent solution of Congo red dye, another sample was withdrawn from the other external jugular vein and treated like the first sample. The tubes were then capped and centrifuged at high speed for forty-five minutes. The hematocrit readings taken directly from these two large graduated centrifuge tubes were averaged. The differences were always slight. The supernatant plasma was then removed with a pipette, and the colors were matched with the standard in the usual way. When a second determination was done within a short time after the first, the remaining dye in the plasma, being incorporated in the standard, did not interfere with the results. The question of hemolysis arose as a possible factor of error in our determinations. We found the qualitative and quantitative spectroscopic methods for its detection too complicated and refined for our purposes. We, therefore, employed a simple guaiac ring test on the plasma which was found adequate to detect any significant amount of hemolysis.* Except for occasional traces which were readily discovered, there was rarely any gross error from this source.

The arterial blood pressure was measured by puncturing the femoral artery with a 19-gauge needle which was attached by a three-way stopcock to a syringe and mercury manometer. We found the mean blood pressure to be very labile. Variations in the depth of anesthesia and therefore in the sensitivity of the aortic depressor and carotid sinus mechanisms[7] might account in part for this lability. It was also thought that the sluice mechanism in the hepatic veins,[8] so active in the dog, might introduce an additional variable in the measurement of systemic arterial blood pressure.

The venous pressure was measured by the direct method.[9] A graduated L-tube washed with 3 per cent citrate solution was attached to a 16-gauge needle which had been inserted into the external jugular vein. The pressure was measured in centimeters of water. Inasmuch as the relation between the level of the external jugular vein and the level of the heart varied in different animals, no absolute values could be established by this method. The relative changes, however, could be fairly accurately determined. The precaution of loosening the upper paws had to be taken since excessive traction occasionally mechanically constricted the veins and gave a high reading. In preoperative and postoperative measurements there was an unavoidable source of error. Despite all efforts to "blow off" the residual pneumothorax when closing the chest, some air was frequently left. With the animal on its back the lungs and mediastinal structures sank toward the back. This made the level of the heart lower with respect to that of the jugular vein than it had been before the operation. This was evident by the greater depth to which the needle had to be inserted in order to reach the heart. Another variable factor was the partial residual pneumothorax due to the thoracotomy. Venous pressure readings in the open chest experiments were, therefore, of questionable significance. In the closed chest experiments these sources of error were eliminated.

*Sunderman and Austin have recently reported a benzidine test for the detection of hemolysis in serum volume determinations (Am. J. Physiol. 117: 474, 1936).

The ether circulation time[10] was measured by injecting 0.5 to 1 c.c. of ether, plus an equivalent amount of physiological saline solution, depending on the size of the dog, into the external jugular vein. The time elapsing between the injection and the detection of the ether in the exhaled air was measured with a stop watch. The chief source of error was a slow respiratory rate. If it was very slow, several seconds might elapse before the alveolar air containing the ether was exhaled. This happened only occasionally, and the error was always noted. Another source of error was infiltration of the fluid outside the vein, a rare accident.

The cyanide circulation time[11] was measured several minutes after the general effects of the ether had been permitted to wear off. One-half to one cubic centimeter of 1 per cent solution of sodium cyanide was used. The time elapsing between the injection of the solution and the onset of deep rapid breathing was recorded with a stop watch. Slowing of the pulse was found to be a less reliable end point. When freshly prepared solutions of this concentration were used, there were rarely any ill effects, even in animals already very sick. The effects of the poison were usually transient, subsiding apparently completely in from five to fifteen minutes, so that subsequently another circulation time could be done without risk. Occasionally the end point was not sharp. These instances were always recorded as such.

The other measurements served as additional checks on our method. The percentage of hemoglobin was read on an ordinary Sahli hemoglobinometer and the erythrocyte count done on a standard hemocytometer. These usually checked with variations in cell volume and arterial blood oxygen. Oxygen saturation was not determined because its estimated value did not seem commensurate with the additional time required. The serum protein determinations were made by the colorimetric method.[12] They served as a rough check on the character and the amount of fluid lost. Temperatures were taken per rectum.

EXPERIMENTAL

A heterogeneous group of mongrel dogs weighing from 10 to 20 kg. were used for these experiments. They varied in age, sex, and nutrition. They were quarantined for two weeks to eliminate those with distemper. One week prior to operation some of the animals were subjected to a series of studies as outlined above. In all dogs similar studies were done before and after operation, and if the animal survived, one day and one week later. At the end of this period the surviving animals were killed.

In order to occlude the anterior descending branch of the left coronary artery, we employed the operative technic described by Gross, Blum, and Silverman.[13] After adequate anesthetization with nembutal (pentobarbital sodium), artificial pulmonary insufflation with a Starling pump was instituted. The chest was opened in the third interspace on the left. The lung was packed down out of the way; the pericardium was incised parallel and anterior to the phrenic nerve; and the anterior descending branch of the left coronary artery was identified. This was carefully dissected as near to its source as possible. It was then ligated in two places with a No. 4 silk thread and severed between ligatures. The pericardium and chest were closed

TABLE I

ANESTHESIA CONTROL EXPERIMENTS

DOG NO.	SEX	PROCEDURE	DATE	WEIGHT IN KG.	TEMPERATURE (F.)	PULSE RATE PER MINUTE	OXYGEN CONSUMPTION IN C.C. PER MINUTE	ARTERIOVENOUS OXYGEN DIFFERENCE, VOLUMES PER CENT	CARDIAC OUTPUT MINUTE VOLUME PER SQ. METER IN C.C.‡	TOTAL BLOOD VOLUME PER SQ. METER IN C.C.‡	HEMOGLOBIN PER CENT	TOTAL SERUM PROTEINS-GRAMS PER CENT	BLOOD PRESSURE		CIRCULATION TIME		REMARKS	
													ARTERIAL IN MM. OF MERCURY	VENOUS IN CM. OF WATER	ETHER IN SEC.	CYANIDE IN SEC.		
63E	♂	Before*	7/14/36	17.3	102.6	196	121.0	2.69	6000	–	87	5.98	135	6.0	4.0	8.0	7/15	Dog died several hours after procedure. Autopsy: Gas gangrene right thigh at site of arterial puncture.
		After†		17.3	103.2	164	156.0	5.07	4108	2280	93	5.79	130	5.5	3.0	8.0		
64E	♂	Before	7/15/36	13.2	105.0	136	125.0	10.28	1945	2220	95	7.06	90	0	6.0	indefinite	7/16	Dog died several hours after procedure. Autopsy: Pneumonia in both lower lobes.
		After		13.2	104.8	140	118.0	6.98	2708	2465	108	7.31	115	3.5	4.5	indefinite		
67E	♂	Before	7/17/36	11.2	100.4	174	93.0	2.07	7915	2243	63	4.94	150	2.5	5.0	6.5	7/18	Dog died several hours after procedure. Autopsy: Pneumonia in left lower lobe.
		After		11.2	100.0	180	92.0	3.25	5000	2020	63	5.08	145	3.0	7.0?	7.5		
70E	♀	Before	7/18/36	12.0	101.9	208	111.0	2.81	6732	2600	89	5.44	145	2.5	6.0	7.5	7/28	Dog apparently well.
		After		12.0	101.6	180	102.0	2.50	6960	2555	84	6.22	130	1.5	3.0	6.0		
		Retested	7/19/36	11.2	102.2	192	96.0	3.10	5460	2459	71	6.15	132	1.0	11.0?	15.0?		
		Retested	7/28/36	11.6	100.6	216	95.0	2.79	5930	2722	92	–	165	4.5	5.0	9.0		

TABLE I—CONT'D

73E	♀	Before	7/20/36	10.2	101.2	168	71.5	2.17	6225	1995	63	5.69	85	3.0	4.0	10.0	7/24	Dog died four days after procedure.
		After		10.2	98.0	168	83.5	2.59	6105	2050	70	5.72	78	–	6.0?	7.0		Autopsy: Atelectatic pneumonic patches both lower lobes.
		Retested	7/21/36	9.9	99.4	132	79.0	3.25	4700	2266	63	8.31	75	2.5	–	–		
74E	♂	Before	7/21/36	9.4	100.3	156	79.0	2.01	7860	2530	69	5.21	95	0	–	7.0	7/29	Dog apparently well.
		After		9.4	99.4	192	77.5	2.00	6750	2436	75	5.09	135	0	3.0	8.0		
		Retested	7/22/36	8.9	99.8	144	59.0	1.58	7782	2488	74	4.03	95	0	3.0	8.0		
		Retested	7/29/36	8.9	100.4	208	79.0	2.15	7500	2185	82	4.36	145	1.5	5.0?	5.0		
80E	♂	Before	7/23/36	11.2	99.8	158	93.0	2.91	5634	2164	59	5.56	145	2.0	4.5	8.0	7/30	Dog apparently well.
		After		11.2	98.4	160	89.0	4.32	3642	1879	63	5.11	150	2.0	4.0	9.0		
		Retested	7/24/36	10.5	101.2	224	104.0	6.47	2973	1574	61	5.10	125	1.0	5.0	9.0		
		Retested	7/30/36	10.2	99.8	214	84.0	5.22	3040	1595	55	5.09	118	–	–	–		
81E	♀	Before	7/24/36	15.0	102.4	200	93.0	2.01	6788	–	91	4.83	125	5.5	4.5	7.0	7/25	Dog died several hours after procedure.
		After		15.0	101.7	164	92.0	2.57	5260	–	95	4.8[illegible]	120	6.0	4.5	8.0		Autopsy: Atelectatic pneumonia left lung.
82E	♂	Before	7/25/36	16.9	100.6	216	134.0	3.74	4838	2273	65	4.13	123	3.0	3.5	6.0	8/1	Dog apparently well.
		After		16.9	100.0	144	124.0	4.84	3460	2380	65	4.06	118	1.0	5.0	8.0		
		Retested	7/27/36	16.7	101.1	208	114.0	4.14	3754	2387	61	3.85	115	5.0	5.0	8.0		
		Retested	8/ 1/36	15.5	101.9	200	115.0	2.72	6065	2728	68	3.92	125	5.5	6.0?	6.5		
10F	♀	Before	8/12/36	21.1	103.0	196	166.0	3.19	6060	3662	91	7.66	140	2.5	4.0	9.0	8/14	Dog died two days after procedure.
		After		21.1	102.8	180	167.0	3.88	5030	3735	91	7.10	130	2.5	4.5	10.5		Autopsy: Small hemorrhagic pericardial effusion, atelectatic pneumonia left upper lobe.
		Retested	8/13/36	20.2	103.6	200	173.0	5.99	3473	3643	97	7.26	130	2.0	5.0	12.0		

*Fifteen minutes after induction of anesthesia.

†Forty-five minutes after induction of anesthesia.

‡Using the Rubner constant for the dog, these values were computed from the Vierordt-Meeh formula, surface area in sq. m. $= 0.112 \times \sqrt[3]{(\text{weight in kg.})^2}$

with silk sutures and the residual pneumothorax "blown off." In the thoracotomy control group, exactly the same operative procedure, including dissection of the coronary branch, was carried out. In these animals, however, the vessel was not ligated.

Complete autopsies were done on all the animals that died or were killed. Each heart was examined, and, if an infarct was found, its size and character were noted. The left anterior descending branch was always probed to determine its patency. If an infarct was present, the heart was injected by the method of Gross[14] to determine its ex-

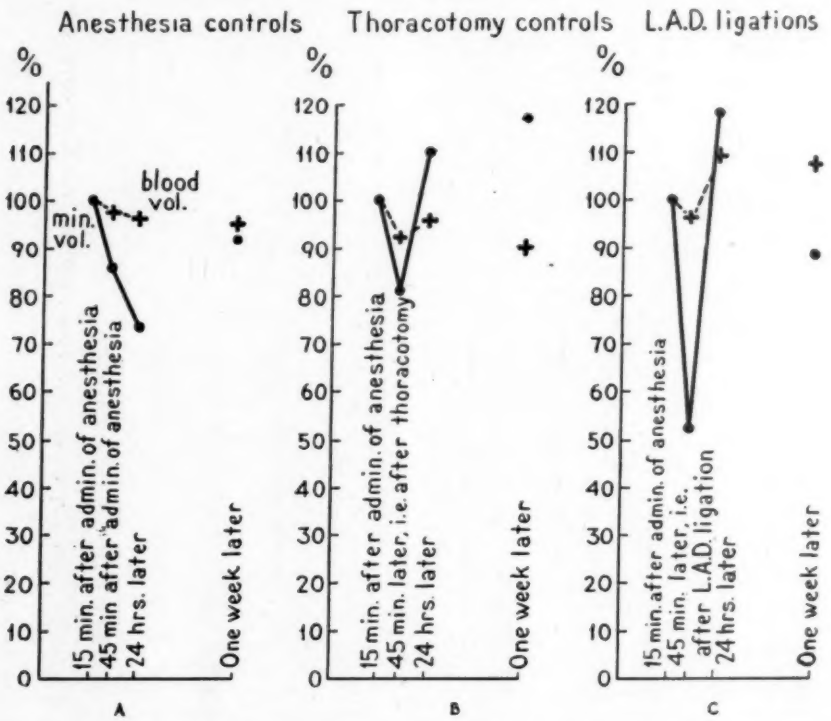

Fig. 1.—Average per cent changes in cardiac output (continuous black line) and in blood volume (dotted line) per square meter of surface area.

tent more exactly. Several of the animals in which the arteries were ligated died of ventricular fibrillation. Others died presumably of shock and pulmonary congestion. The most frequent cause of death in all dogs was pneumonia. Pneumothorax due to lung injury was a less common complication. Wound infection, hemopericardium, pericarditis, empyema, and lung abscess were rare. There was an occasional death following the injection of cyanide.

Table I lists the findings following the administration of anesthesia and therefore serves as a base line for the experiments to be described. Apart from the not inconsiderable fluctuations as between the differ-

ent animals, the only point worthy of note was a moderate immediate fall in average cardiac output. The decrease in average cardiac output became somewhat greater within twenty-four hours (Fig. 1*A*). A week later the average cardiac output was again measured and found to have returned to the original level. The exact time when this return took place was not studied. Figure 2 illustrates the case distribution as to immediate changes in cardiac output in this and in the subsequent experimental groups.

Table II lists the findings in the thoracotomy control group. In these animals, thoracotomy and left anterior descending branch dis-

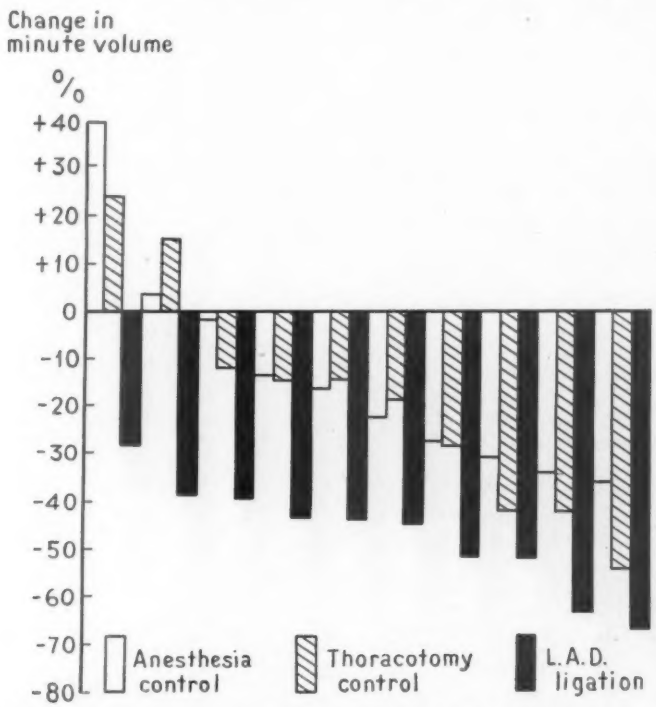

Fig. 2.—Individual case distribution with reference to the changes in cardiac output directly after the procedure.

section (without ligation) were carried out under anesthesia. Hemodynamic studies were made before opening and after closing the chest. As is seen, there was a somewhat greater immediate fall in average cardiac output which, however, tended to rise above the preoperative level within twenty-four hours (Fig. 1*B*). We are inclined to believe that the rise in some dogs in this group (Fig. 2) as well as in the coronary ligation group is* attributable to the partial pneumothorax following the thoracotomy.

*This rise above the preligation level is more apparent than real. Study of a larger series of animals (manuscript in preparation) discloses a twenty-four-hour rise in average cardiac output to almost preligation levels.

TABLE II

THORACOTOMY CONTROL EXPERIMENTS

DOG NO.	SEX	PROCEDURE	DATE	WEIGHT IN KG.	TEMPERATURE (F.)	PULSE RATE PER MINUTE	OXYGEN CONSUMPTION IN C.C. PER MINUTE	ARTERIOVENOUS OXYGEN DIFFERENCE, VOLUMES PER CENT	CARDIAC OUTPUT: MINUTE VOLUME PER SQ. METER IN C.C.	TOTAL BLOOD VOLUME PER SQ. METER IN C.C.	HEMOGLOBIN PER CENT	TOTAL SERUM PROTEINS—GRAMS PER CENT	BLOOD PRESSURE: ARTERIAL IN MM. OF MERCURY	BLOOD PRESSURE: VENOUS IN CM. OF WATER	CIRCULATION TIME: ETHER IN SEC.	CIRCULATION TIME: CYANIDE IN SEC.		REMARKS
60D	♀	Preop.	4/ 1/36	17.0	101.0	172	114.0	2.52	6090	2331	91	6.36	135	4.5	4.0	7.0	4/2	Dog died several hours later. Autopsy: Bilateral lower lobe pneumonia. L.A.D. patent. No infarct.
		Postop.		17.0	98.0	138	104.5	3.25	4325	2311	104	7.77	130	5.0	5.5	11.0		
63D	♀	Prelim.	4/ 2/36	12.8	99.6	196	99.0	5.00	3231	2165	104	-	125	0	4.5	8.0	5/5	Dog died several hours postoperatively. Pneumonia found at operation. Autopsy: Pneumonic patches both lungs. L.A.D. patent. No infarct.
		Preop.	5/ 4/36	12.7	100.6	192	104.5	4.38	3918	2058	90	6.83	125	0	8.0?	10.0		
		Postop.		12.7	100.8	160	102.5	5.05	3334	2008	100	6.97	-	0	9.0?	12.0		
64D	♂	Prelim.	4/ 6/36	21.0	99.0	172	166.0	5.75	3386	2808	98?	7.61	110	7.5?	4.5	9.5	5/4	Dog sacrificed. Moderate hemopericardium found at operation. Autopsy: L.A.D. patent. No infarct. No other abnormalities.
		Preop.	4/22/36	21.9	101.2	194	158.0	9.18	1936	2640	98	6.75	210	9.5?	3.0	15.0?		
		Postop.		21.9	101.0	154	148.0	9.92	1704	2320	93	6.28	170	3.5	5.0	16.5		
		Retested	4/23/36	21.9	100.0	172	156.0	6.34	2810	2233	85	6.82	160	2.5	3.0	10.0		
		Retested	5/ 1/36	19.5	100.8	158	134.0	6.68	2480	2370	75	6.75	145	2.0	7.0?	9.0		
66D	♂	Prelim.	4/ 7/36	21.2	100.0	156	150.5	4.34	4041	2424	88	6.80	163	1.0	4.0	13.0?	5/11	Dog died. Wound ruptured two days before. Autopsy: Gangrenous wound infection. Atelectasis of both lungs. L.A.D. patent. No infarct.
		Preop.	5/ 2/36	21.0	-	220	188.5	3.15	7008	2612	60	6.12	175	3.5	4.0	6.5		
		Postop.		21.0	102.2	206	185.0	5.61	3868	2310	63	6.06	148	3.5	4.0	7.0		

TABLE II—CONT'D

67D	♂	Prelim.	4/ 8/36	12.2	101.4	206	109.0	2.01?	9175?	2620	84	6.74	157	2.0	3.5	8.5	4/24	Dog died one hour postoperatively probably from the combined effect of anesthesia, pneumothorax and the cyanide test. Autopsy: L.A.D. patent. No infarct. No abnormalities.
		Preop.	4/24/36	12.3	–	176	88.0	2.82	5230	2320	80	6.72	135	1.0	4.0	10.0		
		Postop.		12.3	98.0	146	77.5	5.48	2370	2165	83	7.07	118	1.0	6.0	11.0		
86D	♂	Preop.	6/ 3/36	19.8	101.5	185	143.0	4.63	3765	3108	89	6.20	128	1.0	2.5	7.0	6/8	Dog well.
		Postop.		19.8	102.0	164	153.0	6.16	3030	2548	92	6.38	110	3.5	4.0	10.0		
		Retested	6/ 8/36	18.2	–	168	124.0	4.33	3706	2486	82	5.69	110	1.0	4.0	9.0		
		Retested	6/ 8/36	18.2	98.2	136	113.0	3.58	4084	2410	85	5.33	90	3.0	7.0	indefinite		
5E	♂	Prelim.	5/14/36	13.0	99.0	172	106.8	4.36	3950	3300	106	–	148	3.5	13.0?	12.0	5/26	Dog well.
		Preop.	5/21/36	17.9	–	166	103.0	3.52	3790	2680	91	6.09	125	6.5	4.0	9.0		
		Postop.		17.9	95.8	120	101.0	4.08	3220	2430	87	6.12	60	0	18.5?	14.0		
		Retested	5/26/36	16.0	100.0	184	123.0	3.88	4460	2840	97	5.81	118	4.0	9.0?	9.0		
9E	♀	Prelim.	5/16/36	16.1	99.0	196	117.0	2.30	7095	2476	88	–	165	2.5	4.5	9.0	5/25	Dog died four hours postoperatively. Autopsy: Atelectatic pneumonia. L.A.D. patent. No infarct.
		Preop.	5/25/36	16.5	99.8	212	118.0	3.42	4740	2238	91	8.33	150	1.0	3.0	8.0		
		Postop.		16.5	99.0	156	104.0	5.23	2735	2080	93	9.68	112	0	indefinite	11.0		
11F	♂	Preop.	8/12/36	13.3	102.4	180	83.0	5.14	2563	2690	93	–	75	0	5.0	13.0	8/12	Dog died several hours postoperatively. Marked preoperative arterial anoxemia. Autopsy: Pneumonia right lung, probably more than one day old. L.A.D. patent. No infarct.
		Postop.		13.3	101.6	204	93.5	4.67	3175	2436	93	–	115	0	indefinite	13.5		
83F	♂	Preop.	9/29/36	19.0	99.5	172	151.0	3.76	5050	2710	89	6.03	145	3.0	3.0	8.5	9/30	Dog killed because of distemper. Autopsy: Bilateral lower lobe pneumonia. L.A.D. patent. No infarct.
		Postop.		19.0	98.1	140	130.5	2.82	5810	2620	89	5.47	130	3.5	5.0	10.5		
		Retested	9/30/36	18.0	101.7	166	151.0	4.97	3950	3060	99	5.29	100	1.5	4.0	12.0		

TABLE III

LEFT ANTERIOR DESCENDING BRANCH LIGATION EXPERIMENTS

DOG NO.	SEX	PROCEDURE	DATE	WEIGHT IN KG.	TEMPERATURE (F.)	PULSE RATE PER MINUTE	OXYGEN CONSUMPTION IN C.C. PER MINUTE	ARTERIOVENOUS OXYGEN DIFFERENCE, VOLUMES PER CENT	CARDIAC OUTPUT: MINUTE VOLUME PER SQ. METER IN C.C.	TOTAL BLOOD VOLUME PER SQ. METER IN C.C.	HEMOGLOBIN PER CENT	TOTAL SERUM PROTEINS—GRAMS PER CENT	BLOOD PRESSURE: ARTERIAL IN MM. OF MERCURY	BLOOD PRESSURE: VENOUS IN CM. OF WATER	CIRCULATION TIME: ETHER IN SEC.	CIRCULATION TIME: CYANIDE IN SEC.		REMARKS
58D	♂	Preop.	3/28/36	16.0	–	172	112.0	5.75	2738	2358	87	7.00	178	–	3.0	9.5	3/28	Dog died ½ hour postoperatively, apparently from the cyanide test. Autopsy: L.A.D. not patent. No apparent infarct.
		Postop.		16.0	–	154	114.0	10.35	1548	2202	91	6.31	140	–	6.5	15.0		
61D	♀	Prelim.	4/ 2/36	17.5	98.6	174	143.0	4.30	4406	2364	101	7.34	130	–	4.0	8.0	4/16	Dog died several hours postoperatively. Autopsy: Pneumonic patches in left lung. L.A.D. not patent. No apparent infarct.
		Preop.	4/16/36	17.3	–	176	130.5	3.17	5490	2100	93	5.53	155	1.0	4.0	8.0		
		Postop.		17.3	95.8	143	106.0	7.09	1995	2008	72	5.83	120	0	8.0	21.0		
71D	♂	Prelim.	4/10/36	19.2	102.1	130	147.0	3.29	5570	2350	119	7.57	187	–	3.0	7.0	5/11	Dog killed. Autopsy: L.A.D. not patent. Infarct present.
		Preop.	4/25/36	18.7	98.0	192	112.5	3.40	4200	–	88	5.91	170	1.5	4.0	7.0		
		Postop.		18.7	98.0	–	161.0	7.95	2570	–	94	7.34	155	1.0	4.0	8.0		
		Retested	4/27/36	17.8	101.8	215	135.0	2.20	8025	2443	86	6.99	165	3.5	3.0	8.0		
		Retested	5/ 4/36	16.5	99.8	200	108.0	3.01	4940	2312	89	6.75	153	2.5	4.0	7.5		
78D	♂	Prelim.	4/14/36	25.0	100.3	160	147.0	1.72	8920	2520	95	–	145	–	5.0	12.0	5/8	Dog died. Autopsy: Empyema and pericarditis. L.A.D. not patent. Infarct present.
		Preop.	4/28/36	24.0	99.6	180	161.5	2.39	7250	2439	71	7.48	145	3.5	5.0	indefinite		
		Postop.		24.0	98.2	148	152.5	4.03	4060	2458	76	7.09	140	0	3.5	11.0		
		Retested	4/29/36	23.2	101.2	188	157.0	2.81	6450	3100	76	5.85	130	2.5	3.0	indefinite		
		Retested	5/ 7/36	22.0	101.6	162	127.0	3.06	4725	2895	70	4.86	130	8.0	3.5	12.0		

TABLE III—CONT'D

94D	♂	Prelim.	5/11/36	13.6	-	184	103.0	2.18	7380	2870	88	8.00	165	3.0	4.0	7.5	6/2	Dog killed.
		Preop.	5/19/36	12.4	99.0	186	93.0	2.23	6950	2910	80	5.96	155	0	4.0	9.0		Autopsy: Fibrinous pericarditis, partially organized. L.A.D. not patent. Infarct present.
		Postop.		12.4	99.0	156	84.5	6.27	2240	2430	77	5.71	118	2.0	5.5	14.0		
		Retested	5/20/36	12.2	99.0	144	84.0	2.84	5010	2790	71	6.16	-	2.5	-	-		
		Retested	6/ 2/36	10.6	99.0	139	80.0	2.59	5720	3070	64	-	50	10.0	-	-		
1E	♂	Prelim.	5/18/36	19.0	100.6	180	126.0	4.04	3890	2920	85	5.72	135	6.0	4.5	16.0	5/29	Dog died several hours postoperatively.
		Preop.	5/28/36	19.0	99.4	160	114.0	2.17	6570	2650	84	5.55	148	2.0	4.0	10.0		Autopsy: Atelectatic pneumonic patches both lungs. L.A.D. not patent. No apparent infarct.
		Postop.		19.0	98.0	132	97.0	3.87	3140	2420	89	5.81	115	0.5	15.0	20.0		
7E	♂	Prelim.	5/15/36	17.2	101.2	156	112.0	2.63	5760	2519	87	-	143	4.0	7.0	9.5	5/22	Dog died 4 hours postoperatively.
		Preop.	5/22/36	16.2	101.4	168	97.0	2.27	5930	3041	92	-	125	4.0	4.0	9.0		Autopsy: Partial atelectasis left lung. L.A.D. not patent. No apparent infarct.
		Postop.		16.2	98.0	120	92.0	3.94	3240	2663	90	-	80	4.5	5.0	22.0		
8E	♂	Prelim.	5/16/36	16.0	100.6	152	109.0	4.67	3290	3120	92	-	95	0	4.5	10.0	5/23	Dog died several hours postoperatively.
		Preop.	5/23/36	17.0	100.0	160	123.0	3.51	4740	2370	75	5.76	125	7.5	4.0	9.0		Autopsy: Lungs congested. L.A.D. not patent. No apparent infarct.
		Postop.		17.0	99.0	180	108.0	5.14	2840	2390	76	6.93	105	4.0	5.0	11.5		
80E	♂	Preop.	8/10/36	10.5	99.6	184	92.0	4.33	3780	1843	68	5.56	130	1.0	3.5	6.0	8/11	Dog died several hours postoperatively.
		Postop.		10.5	98.0	154	80.2	5.30	2710	1885	68	5.10	100	2.5	-	-		Autopsy: Moderate atelectasis left lung. L.A.D. not patent. Infarct present.
4F	♀	Preop.	8/ 7/36	16.9	101.6	200	118.0	4.48	3553	2144	73	4.47	133	3.5	5.5	12.0	8/8	Dog died several hours postoperatively.
		Postop.		16.9	101.4	180	121.0	9.52	1718	1900	76	5.47	100	3.5	4.0	14.0		Autopsy: Congestion and scattered pneumonic patches in both lungs. Worms in right auricle and ventricle. L.A.D. not patent. No apparent infarct.

Those animals in which the anterior descending branch of the left coronary artery had been ligated presented an immediate decrease in average cardiac output more profound than in either series of controls (Table III). The findings in the individual dogs (Fig. 2) suggest that the diminution in cardiac output occurred consistently. Within twenty-four hours, the average cardiac output rose above* the preoperative level (Fig. 1*C*). Determinations made one week later on two surviving dogs showed a return of the average minute volume to the preoperative level. The immediate decrease in cardiac output was not accompanied by any marked diminution in oxygen consumption. A peripheral effect on metabolism could, therefore, not be held accountable for the diminished minute volume. It was the increase in arteriovenous blood oxygen difference that was usually the important factor. Since the pulse rate showed no consistent variations (a slight average acceleration in the anesthesia control group, as against a moderate average retardation in both of the other two groups) the changes in stroke volume, except for occasional deviations, usually followed those of minute volume. The changes in temperature were frequently directly proportionate to those in cardiac output and oxygen consumption, and inversely proportionate to those in the arteriovenous blood oxygen differences.

The diminution in blood volume was no greater in those dogs whose left anterior descending branch had been ligated than in the control groups. The small decrease often observed was usually at the expense of the plasma volume, there being a corresponding concentration of cells. The relatively slight changes in the percentage of hemoglobin and in the erythrocyte count usually agreed with the changes in cell volume and in arterial blood oxygen. There was rarely any significant change in serum proteins.

Recording of venous pressure, as previously mentioned, was subject to appreciable error. No significant changes were observed. Although fluctuations in mean arterial blood pressure were sometimes extreme, the anesthesia control group on the whole showed negligible changes. The thoracotomy control group, as well as the group with coronary branch ligation, showed an immediate fall in mean arterial blood pressure which averaged 28 mm. of mercury for each group. Inasmuch as both groups showed the same immediate fall, this cannot be attributed to the ligation alone, as was assumed by previous observers. However, the observations on blood pressure recorded here refer, with few exceptions, to preoperative and immediate postoperative levels. These, therefore, do not indicate the possible changes in blood pressure

*This rise above the preligation level is more apparent than real. Study of a larger series of animals (manuscript in preparation) discloses a twenty-four-hour rise in average cardiac output to almost preligation levels.

which may occur twenty-four hours and over after the experimental procedures. Such studies are being conducted at present and will form the basis of a subsequent report.

Ether circulation time also remained relatively unchanged, whereas the cyanide circulation time was moderately prolonged in the thoracotomy control group, but considerably more prolonged following left anterior descending branch ligation. This could be regarded as evidence of congestion in the pulmonary veins. The electrocardiograms were helpful adjuncts to our procedures. The changes that occurred following occlusion of the left anterior descending branch were so characteristic and constant (Gross and Calef[15]) that they were of help in determining the status of the animal in doubtful cases.

DISCUSSION

For reasons mentioned above, no figures are available on the hemodynamic findings in the normal unanesthetized animal. However, if one takes as a base line the changes as observed under anesthesia without operation, it is seen that the only appreciable alterations which follow thoracotomy alone are a tendency for the blood pressure to fall and for the moderately decreased average cardiac output to return to preoperative levels somewhat more rapidly. The additional factor of left anterior descending branch ligation is associated with a moderate immediate fall in average blood pressure. This is similar to that observed in the thoracotomy controls. No definite relation can therefore be established in our experiments between the vascular occlusion and the immediate decrease observed in the mean arterial blood pressure. As mentioned before, these observations on arterial blood pressure refer only to the period immediately following the operative procedures. The average cardiac output, in contrast to the arterial blood pressure changes, showed a definite immediate decrease considerably greater than that observed in either control group. This decrease was also associated with a moderate prolongation of cyanide circulation time. The twenty-four-hour and one-week average values for cardiac output are based on less reliable statistics since the determinations were done on the surviving dogs which represented considerably smaller groups of animals (5 in the anesthesia group, 4 in the thoracotomy group and 3 in the coronary ligation group). The relatively slight differences in average cardiac output between the two control groups is contrary to the reported marked effect of thoracotomy on cardiac output.[16] It was, nevertheless, deemed advisable to eliminate completely the factors introduced by thoracotomy. The results of left anterior descending branch occlusion produced in the closed chest will be subsequently reported.

SUMMARY

1. Methods are described for the study of the hemodynamic changes following left anterior descending coronary branch occlusion.

2. Anesthesia (nembutal) alone, anesthesia and thoracotomy, and left anterior descending coronary branch ligation carried out under anesthesia are accompanied by minimal immediate changes in pulse rate, venous blood pressure, hemoglobin, erythrocyte count, blood volume, and serum proteins. These changes are similar in all three groups. Left anterior descending branch ligation is associated with a moderate immediate fall in mean arterial blood pressure which, however, is no greater than that observed in the thoracotomy control group. Studies on arterial blood pressure twenty-four hours and over after these experimental procedures will be reported subsequently.

3. There is a somewhat greater immediate fall in temperature in the left anterior descending coronary branch ligation group.

4. Ether circulation time remains relatively unchanged, whereas cyanide circulation time is somewhat lengthened following left anterior descending coronary branch ligation.

5. Under anesthesia there occurs a moderate immediate decrease in average cardiac output.

6. After thoracotomy under anesthesia, the immediate decrease in average cardiac output is not significantly different from that under anesthesia alone. Within twenty-four hours the average cardiac output tends to rise to or above preoperative levels.

7. Following ligation of the left anterior descending coronary branch under anesthesia, there is a consistently greater immediate diminution in cardiac output. This also tends to rise to or above preoperative levels within twenty-four hours.

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HEMODYNAMIC STUDIES IN EXPERIMENTAL CORONARY OCCLUSION*

II. Closed Chest Experiments

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IN PREVIOUS reports[1, 2] we have recorded the effects of ligation of the anterior descending branch of the left coronary artery on cardiac output, blood pressure, circulation time, blood volume, and related functions, in the dog. Control observations on the changes in these functions under anesthesia alone and under anesthesia plus thoracotomy revealed a moderate immediate diminution in average cardiac output in both of these series of animals. In spite of the fact that there was no significant difference in immediate average cardiac output as between these two control groups, it was deemed advisable to eliminate the thoracotomy factor at the time of ligation in order to make possible a less complicated appraisal of the circulatory changes after coronary occlusion.

In order to establish a satisfactory technic for acute occlusion of the left anterior descending coronary branch in the closed chest, we experimented with various procedures. The glass cannula of Sutton and Lueth[3] was found to be unsatisfactory because it necessitated the introduction of a rigid tube into the chest with possible limitation of cardiac movement after ligation and with the danger of infection and pneumopericardium. Metal clamps were a possible source of local irritation. It was thought, however, that ligation of the artery from the exterior of the chest could be made feasible by the use of a suitable slipknot. An important feature in the selection of the knot was to have one in which the ends of the threads emerge at opposite points on the chest in order to avoid pulling or rotating the heart by traction on the thread. An adaptation of a double slipknot (the double carrick bend used for reefing) seemed to answer the requirements. Figure 1 illustrates diagrammatically the arrangement of this knot around the coronary vessel.

EXPERIMENTAL

The application of the knot is carried out in the following manner: The chest and pericardium are opened in the usual way. A portion of the anterior descending branch of the left coronary artery near its

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origin is freed by careful dissection. A double thread (No. 2 Pagenstecher linen) is then passed under the vessel with a blunt half curved needle. The knot is made as shown in Fig. 1 and drawn loosely around the vessel by traction of both upper threads against both lower threads. With a straight Hagedorn needle the upper threads are then passed through the anterior pericardium and chest wall to the left of the sternum beyond the edge of the wound. Leaving sufficient slack, the emerging threads are sutured to the skin with one stitch and tied securely. The two posterior threads are passed through the posterolateral pericardium well below the phrenic nerve.

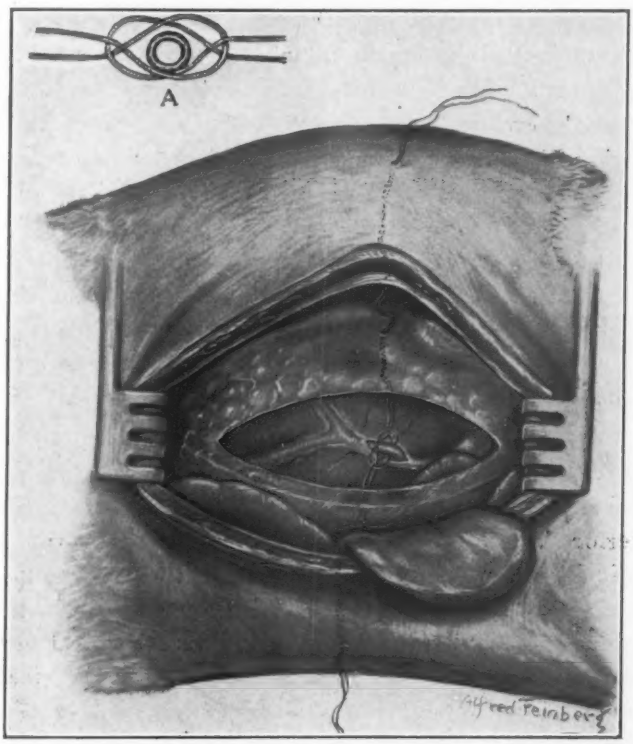

Fig. 1.—The double carrick bend in place on the left anterior descending coronary branch. *A*, Detail of the knot around the artery in cross-section.

They are then passed between the lower and middle lobes of the left lung, and with a long straight Hagedorn needle, brought through the posterolateral chest wall in the fourth or fifth interspace. The emerging threads are sutured to the skin and tied. The pericardium and chest are closed in the usual manner, and a dry gauze dressing is applied and kept in place by a wide adhesive bandage and a dog-jacket made of a towel and safety pins. The artery is ligated one to two weeks after the operation in those dogs which survive this procedure.

The ligation is done under sterile conditions. The slack is eliminated by traction of the anterior two threads against the posterior

two. Any adhesions that have formed are broken in this way. One of the anterior threads is then drawn taut by traction against one of the posterior, following which action the other anterior thread is pulled against the other posterior one. This serves to tighten the double noose gradually and, with several alternations, completely.

The completeness of the vessel occlusion produced in this manner was confirmed by many observations. In only one of the dogs which died before the knot was tied, was the artery found occluded. In one other experiment there was electrocardiographic as well as physiological evidence that the vessel had been occluded by the ligature before the actual manipulation of the threads. In these earlier experiments, insufficient slack had been left. In one animal in which the artery had presumably been ligated, the vessel was found to be patent at autopsy. There was a small pericardial abscess at the site of the knot, causing dissolution of the thread, which in this early experiment was silk and not linen. With these exceptions, the vessel was found to be patent in all animals which died before the knot was tied, and in those dogs in which the artery was ligated there was always electrocardiographic evidence of occlusion. Furthermore, when the latter animals came to autopsy a probe could not be passed beyond the ligature, and if the dog had survived for more than several hours, an infarct could be seen grossly and demonstrated by injection.

The electrocardiogram was usually of considerable aid in determining the cardiac status. As emphasized by Harris and Hussey[4] and recently confirmed by Gross and Calef,[5] the characteristic change after left anterior descending branch occlusion was elevation of the R-T segment in Lead I with or without depression of this segment in Lead III. In one dog, for example, in which the electrocardiogram showed no change and the physiological studies were atypical for occlusion, autopsy disclosed that the noose had accidentally been placed around some muscle fibers and not around the artery, which was patent.

In our control experiments exactly the same procedure was carried out, except that the ligature was placed around some relatively avascular left ventricular muscle near the vessel. Electrocardiographic changes considered characteristic of anterior ventricular wall infarction were never found in these cases.

Ten dogs were used for the control experiments and ten dogs for the left anterior descending branch ligation. In both groups a series of studies was carried out on the hemodynamics of the circulation similar to those described in the previous report. These studies were made under anesthesia before and after traction on the external sutures, one day later and one week later.

As shown in Table I, the results following ligation of a small portion of myocardium by traction on the sutures outside the chest were not appreciably different from those described in the previous report[2] following anesthesia alone or anesthesia plus thoracotomy. There was a moderate immediate decrease in the average cardiac output which remained at approximately the same level at the end of twenty-four hours (Fig. 2*A*). No further studies were made until one week later, when the average minute volume was found to be considerably above the preligation level, due, presumably, to the associated relative anemia which these animals developed.

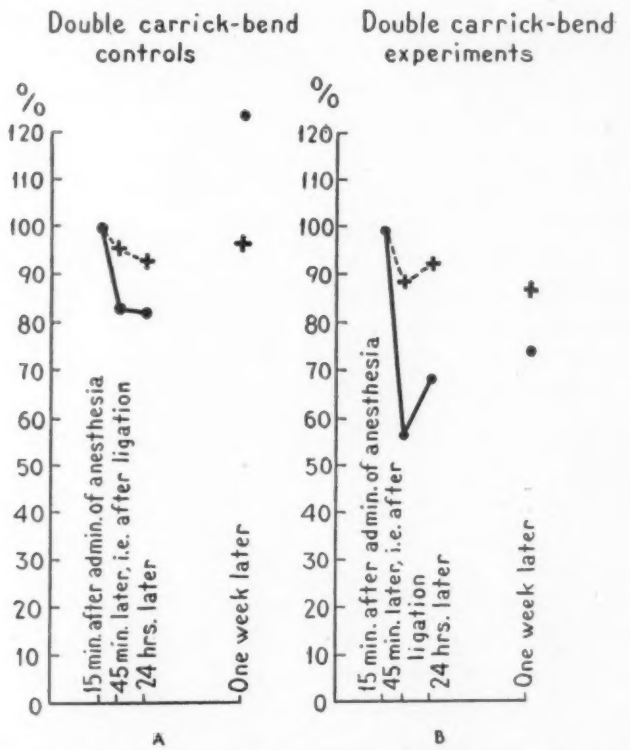

Fig. 2.—Average per cent changes in cardiac output (continuous black line) and in blood volume (dotted line) per square meter of surface area.

Similarly (Table II), ligation of the left anterior descending branch by traction on the sutures outside the chest was followed by essentially the same immediate changes in cardiac output (Fig. 2*B*) as occurred in the dogs in which ligation was performed in the open chest.[2] Immediately after ligation of the vessel there was a decrease in average cardiac output more profound than in the control group. The cardiac output of individual dogs showed this decrease consistently (Fig. 3). Twenty-four hours later, the average output had risen somewhat but had not yet reached preoperative levels. One

TABLE I

DOUBLE CARRICK-BEND CONTROL EXPERIMENTS

DOG NO.	SEX	PROCEDURE	DATE	WEIGHT IN KG.	TEMPERATURE (F.)	PULSE RATE PER MINUTE	OXYGEN CONSUMPTION IN C.C. PER MINUTE	ARTERIOVENOUS OXYGEN DIFFERENCE, VOLUMES PER CENT	CARDIAC OUTPUT: MINUTE VOLUME PER SQ. METER IN C.C.	TOTAL BLOOD VOLUME PER SQ. METER IN C.C.	HEMOGLOBIN PER CENT	TOTAL SERUM PROTEINS—GRAMS PER CENT	BLOOD PRESSURE: ARTERIAL IN MM. OF MERCURY	BLOOD PRESSURE: VENOUS IN CM. OF WATER	CIRCULATION TIME: ETHER IN SEC.	CIRCULATION TIME: CYANIDE IN SEC.	REMARKS	
86D	♂	Prelig.*	6/ 8/36	18.2	-	168	124.0	4.33	3706	2486	82	5.69	110	1.0	4.0	9.0	6/8	Dog died 2½ hours after ligation. Autopsy: hemorrhagic effusion in both pleural cavities; L.A.D. patent; no infarct.
		Postlig.		18.2	98.2	136	113.0	3.58	4084	2410	85	5.33	90	3.0	7.0	-		
84E	♂	Prelig.	8/ 3/36	11.9	101.0	196	87.0	4.66	3200	2256	94	4.38	125	1.5	4.0	9.0	8/3	Dog died ½ hour after ligation. Autopsy: L.A.D. patent; no infarct.
		Postlig.		11.9	99.6	200	83.0	6.97	2040	2118	99	4.48	130	2.5	5.0	15.0		
88E	♀	Prelig.	8/ 4/36	12.4	103.4	160	95.0	3.96	4000	2078	84	4.88	95	2.0	6.0	8.0	8/4	Dog died 2 hours after ligation. Autopsy: atelectatic pneumonia both lungs; L.A.D. patent; no infarct.
		Postlig.		12.4	103.4	166	91.0	4.94	3070	2330	84	4.69	95	1.0	3.5	9.5		
89E	♂	Prelig.	8/ 5/36	15.0	101.4	178	99.0	5.30	2740	2515	86	3.98	150	-	5.0	12.0	8/20	Dog apparently well.
		Postlig.		15.0	102.0	182	104.0	8.60	1776	1910	88	4.04	155	1.0	7.0	-		
		Retested	8/ 6/36	15.0	102.0	168	101.5	-	-	2322	86	4.43	90	-	5.0	8.0		
		Retested	8/14/36	15.0	102.1	176	105.0	4.18	3690	2193	72	4.30	130	2.5	5.0	12.0		

*Ligation of left ventricular muscle.

TABLE I—CONT'D

90E ♀	Prelig.	8/ 6/36	11.4	99.6	152	91.0	4.39	3633	1705	80	6.31	95	3.0	4.0	7.0	8/7	Dog died 1 day after ligation. Autopsy: pneumonic patches both lungs; L.A.D. patent; no infarct.
	Postlig.		11.4	98.2	158	77.0	5.18	2608	1648	85	5.66	115	2.5	–	8.0		
96E ♂	Prelig.	8/13/36	12.4	102.6	200	94.0	3.74	4192	2272	90	5.65	135	0	6.0	8.5	8/24	Dog died several hours after second retesting. Autopsy: small pneumonic patches in right lung; L.A.D. patent; no infarct.
	Postlig.		12.4	102.6	184	98.0	4.13	3957	2040	87	5.42	140	0	5.0	12.0		
	Retested	8/15/36	11.8	103.6	210	109.0	4.33	4340	2060	70	5.51	145	0	–	12.0		
	Retested	8/22/36	12.2	101.0	186	80.0	3.31	4073	1965	66	–	125	2.5	4.0	12.0		
97E ♂	Prelig.	8/14/36	10.8	102.2	180	108.0	3.51	5560	2070	72	4.54	135	0	3.5	10.0	8/15	Dog died of overanesthesia 1 day after ligation before first retesting could be completed. Autopsy: L.A.D. patent; no infarct.
	Postlig.		10.8	102.6	180	101.0	4.32	4220	2052	70	4.74	118	0	4.0	12.0		
98E ♂	Prelig.	8/17/36	15.7	103.1	162	122.0	1.87	9290	2545	70	4.34	165	4.5	4.0	14.0	8/20	Dog died 1 day after last retesting, at which time there was a marked arterial anoxemia. Autopsy: pneumonic patches both lungs; L.A.D, patent; no infarct.
	Postlig.		15.7	102.8	214	117.0	2.13	7825	2156	70	4.52	155	4.5	4.0	14.0		
	Retested	8/18/36	14.9	102.1	162	106.0	–	–	1850	70	4.52	115	3.5	3.5	14.0		
	Retested	8/19/36	14.9	102.2	130	104.0	5.21	2940	2042	68	4.03	58	2.5	4.0	11.5		
100E ♂	Prelig.	8/17/36	11.2	102.4	138	85.5	3.39	4495	2054	72	4.80	103	3.0	–	11.5	8/24	Dog apparently well.
	Postlig.		11.2	101.7	120	87.0	4.56	3400	2256	72	5.37	88	2.5	5.0	10.5		
	Retested	8/19/36	11.4	101.7	130	86.0	2.98	5080	2340	63	5.45	78	1.5	4.0	12.0		
	Retested	8/24/36	11.0	102.1	106	86.0	2.98	5200	2253	57	–	108	9.0	–	–		
1F ♂	Prelig.	7/18/36	12.0	100.4	142	97.5	3.72	4465	2168	88	6.12	110	2.5	4.0	11.0	8/24	Dog apparently well.
	Postlig.		12.0	99.2	136	92.0	3.14	4995	2225	90	5.63	110	2.5	6.0	19.5		
	Retested	8/19/36	11.7	100.8	144	89.5	4.30	3600	1950	87	5.43	68	2.5	6.5	11.0		
	Retested	8/24/36	11.7	101.6	164	117.0	3.08	6550	2270	66	–	125	2.5	3.5	6.5		

TABLE II

DOUBLE CARRICK-BEND EXPERIMENTS

DOG NO.	SEX	PROCEDURE	DATE	WEIGHT IN KG.	TEMPERATURE (F.)	PULSE RATE PER MINUTE	OXYGEN CONSUMPTION IN C.C. PER MINUTE	ARTERIOVENOUS OXYGEN DIFFERENCE, VOLUMES PER CENT	CARDIAC OUTPUT: MINUTE VOLUME PER SQ. METER IN C.C.	TOTAL BLOOD VOLUME PER SQ. METER IN C.C.	HEMOGLOBIN PER CENT	TOTAL SERUM PROTEINS—GRAMS PER CENT	BLOOD PRESSURE: ARTERIAL IN MM. OF MERCURY	BLOOD PRESSURE: VENOUS IN CM. OF WATER	CIRCULATION TIME: ETHER IN SEC.	CIRCULATION TIME: CYANIDE IN SEC.	REMARKS
15E	♂	Prelig.*	6/17/36	10.8	99.0	155	69.0	3.66	3412	2452	70	5.81	93	2.0	–	13.0	6/19 Dog died after first retesting. Autopsy: lungs congested; scattered atelectatic pneumonic patches; L.A.D. not patent; infarct 4 × 4 cm.
		Postlig.		10.8	97.2	138	69.0	5.77	2165	1854	70	6.04	120	1.0	–	18.0	
		Retested	6/18/36	10.5	100.4	140	85.0	6.13	2563	1916	58	5.31	60	1.0	4.0	30.0	
81D	♂	Prelig.	6/22/36	15.7	99.0	168	113.5	4.44	3645	2957	75	–	113	1.0	6.0	9.5	6/23 Dog died several hours after ligation. Autopsy: slight wound infection; lungs congested; L.A.D. not patent; no apparent infarct.
		Postlig.		15.7	97.0	152	109.0	5.90	2634	2735	75	5.56	133	0.5	5.5	10.0	
84D	♂	Prelig.	6/23/36	11.2	97.2	196	99.0	3.82	4569	2283	75	4.38	135	0	3.5	8.0	6/30 Dog died of overanesthesia after second retesting. Autopsy: several atelectatic patches both lower lobes; L.A.D. not patent; infarct 2 × 3 cm. with aneurysmal dilatation.
		Postlig.		11.2	95.0	168	75.0	3.80	3479	2458	75	4.48	100	1.0	5.0	10.0	
		Retested	6/24/36	10.8	100.2	152	96.0	3.08	5645	2175	60	–	65	1.0	4.0	13.0	
		Retested	6/30/36	11.1	–	180	102.5	2.41	7540	–	61	–	105	7.0	–	–	
85D	♂	Prelig.	6/24/36	15.9	100.4	170	116.5	2.48	6620	–	72	–	135	3.0	6.0	10.0	6/24 Dog died of ventricular fibrillation before 2nd series of tests could be completed. Autopsy: L.A.D. not patent; no apparent infarct.
		Postlig.		15.9	–	152	114.0	3.94	4078	–	–	–	147	–	–	–	

*Ligation of L.A.D. coronary branch.

*Ligation of L.A.D. coronary branch.

TABLE II—CONT'D

35E	♂	Prelig.	6/25/36	14.0	98.5	188	106.0	1.75	9268	2605	62	5.00	135	2.5	4.0	8.5	7/1	Dog killed. Autopsy: lungs congested; L.A.D. not patent; infarct present; roundworms in right auricle and ventricle.
		Postlig.		14.0	96.8	88	99.0	5.64	2683	1908	57	5.12	115	0	5.5	12.0		
		Retested	6/26/36	13.8	100.2	166	127.0	4.05	4845	2308	49	5.77	75	2.0	6.0	16.0		
		Retested	6/30/36	12.0	102.1	172	121.0	3.20	6405	2148	59	4.43	99	0	5.0	9.0		
39E	♂	Prelig.	6/26/36	12.4	99.0	168	95.5	4.81	3308	2658	64	5.82	120	0	4.0	8.5	6/27	Dog died of overanesthesia before 1st retesting could be done. Autopsy: L.A.D. not patent; infarct present.
		Postlig.		12.4	97.4	130	79.0	8.82	1490	2300	74	6.50	95	3.5	7.0	17.0		
38E	♂	Prelig.	6/29/36	–	99.4	168	106.0	2.07	–	–	76	6.52	110	3.5	3.0	10.0	6/29	Dog died one-half hour after ligation. Autopsy: preexisting pneumonia with small empyema; L.A.D. not patent; no apparent infarct.
		Postlig.		–	97.0	160	90.0	4.20	–	–	82	6.82	100	3.5	–	9.0		
22F	♂	Prelig.	8/26/36	18.4	102.6	202	151.0	3.00	6450	2810	76	4.36	120	0	4.5	9.5	8/27	Dog died 3 hr. after 1st retesting. Autopsy: pneumonic patches both lungs; L.A.D. not patent; no apparent infarct.
		Postlig.		18.4	102.0	208	133.0	3.98	4280	2730	76	4.46	118	1.0	4.0	13.0		
		Retested	8/27/36	17.6	103.6	170	165.5	6.20	3515	3000	77	3.93	85	2.5	10.0	15.0		
58F	♂	Prelig.	9/23/36	11.6	99.8	166	94.0	1.88	8700	2450	65	3.82	90	0	4.0	10.0	10/2	Dog killed. Autopsy: L.A.D. not patent; infarct present.
		Postlig.		11.6	98.2	189	79.5	3.30	4180	2026	74	4.12	125	1.0	4.0	10.5		
		Retested	9/24/36	10.9	100.4	142	95.0	5.17	3330	2420	67	3.63	70	1.0	4.5	14.0		
		Retested	10/ 1/36	11.2	100.8	144	111.0	2.84	6975	2253	60	2.56†	95	3.5	7.5†	11.5		
26G	♀	Prelig.	10/24/36	12.0	101.4	215	114.0	4.69	4140	2426	81	6.23	130	3.0	6.0	10.5	10/25	Dog died 24 hr. after ligation. Autopsy: moderate bilateral hemorrhagic pleural effusion; pneumonia left lower lung; L.A.D. not patent; infarct present.
		Postlig.		12.0	99.0	166	104.0	7.33	2420	2240	84	5.79	143	0.5	–	14.5		

week later, the average minute volume was closer to the preligation level. The twenty-four-hour and the one-week average values represented fewer animals and were therefore considered less reliable.

The changes in the other functions were also similar to those observed in our previous experiments.[2] The temperature, usually in direct ratio to the minute volume, was lower after ligation of the artery than in the control dogs. The arteriovenous oxygen difference, usually in inverse ratio to the cardiac output, was greater after ligation of the vessel than after ligation of ventricular muscle. Although there was a moderate prolongation of cyanide circulation time in some

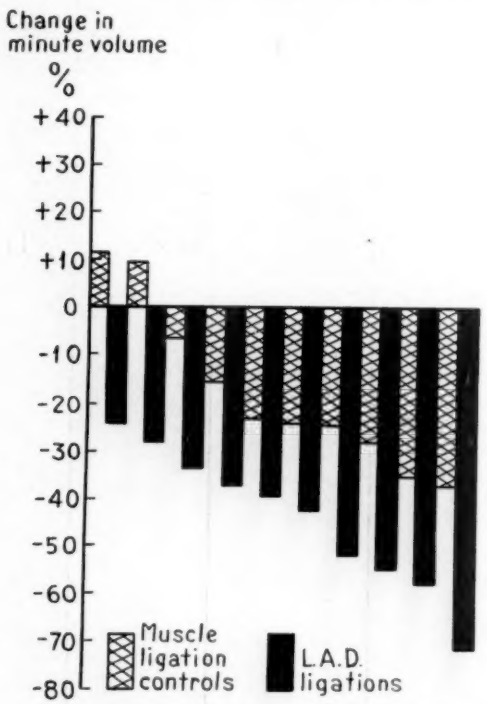

Fig. 3.—Individual case distribution with reference to the changes in cardiac output directly after the procedure.

of the control animals, this was usually more marked in those dogs in which the vessel was ligated. There was no significant change in ether circulation time. The blood volume was usually slightly diminished in both groups, and the changes in hemoglobin percentage and in erythrocyte count usually coincided with those in cell volume. The serum proteins remained relatively unchanged. The average pulse rate was moderately retarded in the animals in which the vessel was ligated. The average immediate changes in blood pressure were approximately the same as in the anesthesia controls previously described.[2] There was no immediate decrease in the average mean arterial blood pressure in either group such as was observed in our thoracotomy controls or after

ligation in the open chest. The observations on arterial blood pressure made twenty-four hours and over after ligation of the artery or of myocardial fibers (control) suggest a fall in blood pressure in both groups of experiments which exceeded that found in the anesthesia and thoracotomy controls. The number of animals on which these blood pressure readings were made was too small to warrant definite conclusions. A more extended series of such studies will be reported elsewhere.

Although the venous pressure was not subject to the errors introduced by thoracotomy, i.e., alteration in the position of the heart and increased intrathoracic pressure because of residual pneumothorax, it did not change consistently with coronary artery ligation. It must be remembered that the venous pressure, like the arterial pressure, represents a balance of two opposite forces. One is the head of pressure remaining after the blood has traversed the capillaries, plus any additional pressure afforded by the tone of the venous vessel walls and of the surrounding muscles. The other is the resistance encountered in the chest and heart, plus or minus the hydrostatic pressure, depending upon the level at which the venous pressure is measured in relation to the heart. Since the hydrostatic factor is constant in our experiments, it can be considered eliminated for comparative purposes. The competence of the venous valves is another factor which, for our purposes, can be neglected. In our experiments, then, the diminution in cardiac output would tend to reduce the residual head of pressure in the veins. The congestion in the pulmonary circuit would, however, tend to increase the pressure in the right heart and therefore offer resistance to venous inflow. The venous pressure reflecting the balance of these forces could, therefore, reasonably be expected to be variable.

DISCUSSION

From the above mentioned findings, it is apparent that the effect of thoracotomy on the factors studied was negligible. The principal changes after experimental occlusion of the anterior descending branch of the left coronary artery in the closed chest experiments were similar to those in the open chest experiments. They consisted of an immediate diminution in cardiac output and an increase in cyanide circulation time. The diminution in cardiac output, in our opinion, represents what Harrison[6] terms hypokinetic circulatory failure despite the inconsistent variations in arterial and venous blood pressure. The prolonged cyanide circulation time, in the absence of significant changes in ether circulation time and venous pressure, is evidence of congestion in the pulmonary veins. The relatively insignificant immediate changes in the arterial blood pressure suggest that, for at least a short period following coronary occlusion, a peripheral vasoconstriction in the dog compensates for the diminution in cardiac output. Experiments subsequently to be described afford evidence to support this view. A limited

number of figures available suggest that twenty-four hours after the coronary ligation (possibly also after muscle ligation) there occurs a fall in blood pressure. This point will be reported elsewhere on a more extensive series.

The observations on cardiac output following experimental coronary occlusion suggest that we are dealing with a combination of left ventricular congestive failure and hypokinetic circulatory failure. Whether the latter represents true "forward failure," that is, whether it is entirely cardiogenic, is still open to question. The absence of blood volume changes rules out the possibility that the diminished output is hematogenic, i.e., caused by loss of blood or plasma in or about the injured myocardium, or that it is vasogenic, i.e., due to a similar loss because of a deleterious effect on peripheral capillaries in general. The neurogenic hypothesis still remains to be considered. The occurrence of a consistent diminution in cardiac output as well as the fact that this diminution occurred while the animal was under anesthesia affords some evidence against this possibility.[7] In order to rule it out completely, a similar series of studies was carried out in dogs with denervated hearts. This will form the subject of a subsequent report.

SUMMARY

1. A method for ligating the anterior descending branch of the left coronary artery from the exterior of the chest is described.

2. The changes in circulation following this procedure were:

   a. Hypokinetic circulatory failure (diminished cardiac output).

   b. Left ventricular congestive failure (increased cyanide circulation time).

3. Because of the absence of any corresponding decrease in blood volume the diminished cardiac output could not be considered to be either hematogenic or vasogenic.

4. Indirect evidence against the neurogenic hypothesis is also presented.

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THE DIAGNOSIS OF IMPENDING ACUTE CORONARY ARTERY OCCLUSION*

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IT IS well recognized that acute coronary artery occlusion is often preceded for months or years by attacks of characteristic angina pectoris. Even prior to the time that Herrick,[1] Dock,[2] and others defined the syndrome of acute coronary artery occlusion, the diagnosis of angina pectoris carried with it the grave possibility of sudden death especially as a sequel to "angina pectoris decubitus."

In contrast to the occurrence of progressive angina pectoris, it has been apparent to us, on observation of a series of cases extending over two and one-half years, that a single spontaneous attack of prolonged anginal pain strongly suggests the approach of a typical coronary thrombosis. Certain characteristics of these attacks of pain seemed to be so well defined that several individuals were put to bed either at home or in a hospital from one to fourteen days prior to the development of the typical symptoms and signs of the arterial block.

Levine[3] summarized those elements in the patients' history that commonly seemed to precede the attack, especially emphasizing mild general discomfort and fatigue. Conner and Holt[4] and Parkinson and Bedford[5] describe the occurrence of transitory pains in the chest of a nature different from previous anginal attacks. These pains occasionally precede the typical coronary artery occlusion. Herrick[1] mentions in one of his case histories a premonitory attack of pain of unusual nature arising three days prior to the occlusion. Feil[6] in a recent personal communication stated that he had assembled a group of cases similar to those we are presenting which indicated to him the importance of this premonitory symptom.

An interesting clinical comparison may be drawn between the diagnosis of impending coronary artery occlusion and impending occlusion of an intestinal artery. Dunphy[7] defined the typical features of the latter condition and quoted a case history of premonitory pain occurring two months prior to death from the acute block of gradually thrombosing celiac axis and inferior mesenteric arteries.

Benson[8] and others have described sclerotic coronary arteries which, though narrowed to a minute anatomical pathway, still carry a stream of blood. Such small channels can carry conceivably only inadequate supplies. Because of varying dynamic factors, this reduced flow may

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be temporarily insufficient to maintain normal myocardial function and may thus produce pain. It is the prevalent opinion that blockage occurs less frequently in arteries of good aperture than those that have been gradually narrowed to an extreme degree. Special importance is placed on this process in encouraging the development of collateral coronary circulation by Beck,[9] Wearn and his associates,[10] and Gross and Kugel.[11] Therefore it is unnecessary to assume that pain of a more prolonged and possibly different character than earlier angina pectoris must be produced by an anatomically closed arterial lumen. It may be expected that a vessel narrow enough to produce this warning would shortly become completely thrombosed. With a rich col-

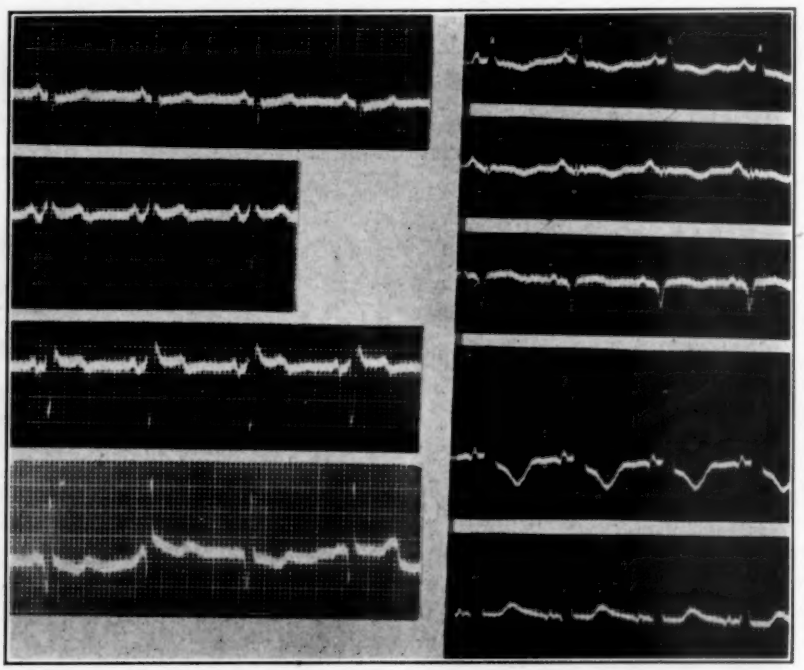

Fig. 1.—Mr. S. (Case 25). First record, April 13, 1936, prior to coronary artery occlusion. Second record, Aug. 31, 1936, two days after coronary artery occlusion. Two Lead IV strips are illustrated in the second record: the first was made with the anterior chest electrode immediately to the left of the sternum in the fifth interspace, the second record, immediately medial to the cardiac apex impulse.

lateral blood supply, acute symptoms and signs of the blockage may never develop. This may account for the rare "silent coronary occlusion" seen at autopsy.

CASE REPORTS

To illustrate the type of cases summarized in Table I and which will be discussed later, the histories and findings of two of the twenty-nine cases reviewed, are outlined:

CASE 25.—Mr. S., aged sixty-five years, first developed squeezing central substernal pain radiating into the left arm on strenuous exertion, i.e., hill climbing, two years

prior to the present illness. This pain gradually increased in severity, duration, and ease of onset over a period of four months until he would have a paroxysm radiating into his left upper arm on walking one block on level ground.

His activity was then restricted to short walks, and he was troubled by pain on such effort only after a moderately large meal. This state remained fairly constant, and with rest ordered after meals and small frequent feedings, he was maintained almost free of pain attacks.

For two weeks prior to admission to the hospital he complained of sudden recurrence of mild attacks of pain of similar distribution, on the effort of walking 30 to 50 feet in his home. These lasted only a minute or less and were relieved by nitroglycerin, gr. $\frac{1}{200}$. Three days before admission, while at rest in bed at night, he suddenly developed a similar but severe attack that lasted forty-five minutes

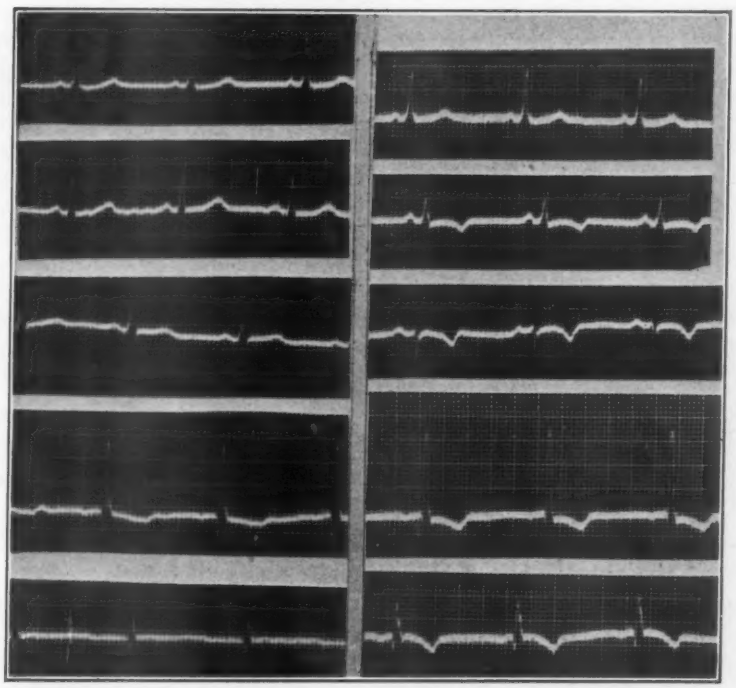

Fig. 2.—Mr. V. (Case 28). First record, Sept. 8, 1936, twenty-four hours prior to the attack during the premonitory phase. Second record, Sept. 14, 1936, five days after onset of acute coronary artery occlusion.

and was only partially relieved by two doses of nitroglycerin. He was kept at complete rest but the next day had four paroxysms of milder nature lasting from two to five minutes, and the succeeding day had absolutely no pain. At 11:00 P.M. the night before admission he developed a violent crushing central substernal pain that was not relieved by nitroglycerin and persisted for sixteen hours with varying intensity until relieved by subcutaneous morphine administration after admission into the hospital. The subsequent course of this patient was characteristic of acute coronary artery occlusion. His blood pressure, which had been 164/108 on the day prior to hospital admission, fell to 94/90 on the day after admission. His leucocyte count two days after admission was 14,850. For four days after entry into the hospital, his temperature was elevated, with a maximum of 38.2° C. registered on the second day after admission. His electrocardiograms taken one month prior to and ten days after admission are shown in Fig. 1.

CASE 28.—Mr. V., aged fifty-one years, a tailor, had been observed, seven years prior to his present illness, in a characteristic attack of acute coronary occlusion. His recovery had been complete, with the exception of lingering but transient albuminuria.

Forty-eight hours before entry to the hospital, he had a severe attack of precordial pain lasting between ten and fifteen minutes, occurring while at work (sedentary). The pain was squeezing in nature and was located across the anterior chest from the second to the fourth ribs, and it did not radiate. There was no pain during the remainder of that day or during the next, even on climbing stairs and walking fairly rapidly.

On the morning of admission he awoke at 7:00 A.M. with a mild sense of precordial distress which decreased after he had dressed himself, but did not entirely clear. When he had reached his tailor shop, the pain suddenly became violent, and he was sent to the hospital. The pain lasted about forty-five minutes, but on arrival at the hospital it had cleared completely. He had no fever, leucocytosis or further pain for forty-eight hours following. His erythrocyte sedimentation rate was three and one-half hours for 18 mm. (technic of Linzenmeier) on the day of admission, and his electrocardiogram was not strikingly abnormal (Fig. 2). Forty-eight hours after admission, while at complete rest in bed, he developed severe precordial pain of similar nature and distribution as before. The pain persisted for ten hours, requiring three doses of morphine sulphate, gr. ¼, administered subcutaneously, to control it.

His course for the next week was marked by a febrile temperature range, a definite leucocytosis of 18,000, a gradual shortening of the sedimentation rate to 35 minutes for 18 mm. on the fifth day after the prolonged pain attack (Rabinowitz and his coworkers,[12] Wood[13]) and on the seventh day, definite changes of the Q_3-T_3 type in the electrocardiogram (Parkinson and Bedford[14]).

OBSERVATIONS AND DISCUSSION

Table I summarizes certain features of twenty-nine cases presenting what we believe to be evidence of impending coronary artery occlusion. As will be seen from this table, these cases were distributed, with regard to age and the particular coronary artery branches involved, in about the same frequency as noted in the reported summaries of other authors. The diagnosis of the location of the block in the coronary arterial system was made in four cases by autopsy, and otherwise presumptively from the electrocardiogram.

Thirteen of the twenty-nine cases were observed in the Mount Zion Hospital during a period when, in this same hospital, fourteen other cases of acute coronary artery occlusion not presenting recognized premonitory pain were diagnosed. The percentile incidence of the thirteen cases with premonitory pain, in the total hospital series of twenty-seven cases of acute coronary occlusion, was 48.1 per cent; thus approximately half of all the cases had premonitory attacks of pain.

In the twenty-nine cases reviewed in this paper (Table I), long-standing angina pectoris was scarcely more common than it was in the twenty-seven cases of coronary occlusion studied at the Mount Zion Hospital. In the former series the percentile frequency of prolonged anginal attacks was 44.8 per cent; in the latter series, 48.1 per

cent. These percentages vary little from those given in other statistics on this subject; Conner and Holt[4] found a 38 per cent incidence of angina pectoris in their series of cases of acute coronary artery occlusion. In the patients in our series (Table I) presenting a history of angina pectoris, the average duration was thirteen and one-half months, the longest being four years.

The character of the premonitory attack of precordial pain observed in those patients who had had angina pectoris previously rarely differed from their former pain either in its nature—i.e., squeezing, crushing, etc.—or in radiation. However, there were at least two cases presenting a definite change in the nature and radiation of the pain. The effect of nitroglycerin on the premonitory attack was definitely transient, with failure of complete relief even on repeated doses although opportunity to observe this effect did not arise frequently.

As summarized from column 8 of Table I, the duration of the warning attack varied from 2 minutes to 2 hours, averaging 63 minutes in individuals without a history of angina pectoris; and from 15 minutes to 14 hours, averaging 2 hours and 40 minutes in patients with that history. However, in the whole series of 29, there were only 7 patients who had pain of less than 20 minutes' duration. Of these, three were individuals who had had progressively severe anginal attacks occurring after shorter interludes and with decreasing amount of effort, but who had not had pain when at rest. In this series no premonitory attacks occurred during sleep, and strenuous exertion occasionally preceded the pain. The attacks generally subsided suddenly and spontaneously without the use of opiates.

Two patients (Cases 16 and 23), aged forty-five and fifty-one years, both males, had precordial pain which sometimes did and sometimes did not occur on effort. Onset of the pain occurred three weeks and five weeks, respectively, prior to the prolonged spontaneous attack that is indicated in the table as the characteristic premonitory symptom of occlusion of the artery. Such cases of inconstant pain, especially when accompanied by normal electrocardiograms, present serious diagnostic problems. Perhaps this clinical picture should be recognized as an equally important precursor to coronary thrombosis as single prolonged spontaneous attacks of pain. The influence of absolute bed rest on prognosis will be mentioned later, but is interesting to consider in respect to these two cases. Patient 16 was allowed to attend to his ordinary business affairs, and Patient 23 was put to bed. However, each died within a few hours after the development of the actual arterial occlusion.

The interval between the premonitory attacks and the major attacks of patients in the entire series, varied between 1 day and 21 days; and

TABLE 1

ANALYSIS OF 29 CASES PRESENTING THE PREMONITORY SYNDROME OF ACUTE CORONARY ARTERY OCCLUSION

CASE NO.	AGE	SEX	BEFORE PREMONITORY ATTACK			INTERVAL BETWEEN PREM. AND ACTUAL OCCLUSION	APPROXIMATE DURATION OF PREMONITORY ATTACK	CONDITION PREMONITORY BEFORE OCCLUSION	ELECTROCARDIOGRAMS	OUTCOME
			NO ANGINA	PROGRESSIVE ANGINA	ANGINA PECTORIS DURATION					
1	62	M	–	–	6 mo.	2 wk.	3 hr.	Asymptomatic	After occlusion: Inversion T_1 and T_2.	Alive
2	45	M	+	–	–	3 wk.	20 min.	Asymptomatic	After occlusion: A-V block; complete left bundle-branch block.	Dead (L. ant. desc. art. occluded)
3	60	F	+	–	–	3 days	Vomited once ± 10 min.	Slight dyspnea	After occlusion: Left bundle-branch block.	Dead (L. ant. desc. art. occluded)
4	63	M	+	–	–	4 days	Burning in chest ± 15 min.	Asymptomatic	After occlusion: Q_1-T with inverted T_3 (anterior lesion).	Alive
5	48	M	+	–	–	2 wk.	1½ hr.	Asymptomatic	After occlusion: Depressed S-T_1 and S-T_3; absent Q_4.	Dead (no autopsy)
6	38	M	–	–	3 yr.	3 days	14 hr.	Asymptomatic	After occlusion: Fusion S-T_1, S-T_2 and S-T_3.	Alive
7	58	M	+	–	–	3 days	2 hr.	Asymptomatic	After occlusion: Q_1-T type.	Alive
8	59	M	–	–	1 yr.	1 wk.	10 min.	10 min. anginal attacks	After occlusion: S-T_2, S-T_3 fused.	Alive
9	71	M	+	–	–	2 days	Not known	Asymptomatic	After occlusion: Auricular fibrillation; flat T_1, T_2 and T_3; absent Q_4.	Alive
10	65	M	–	–	3 mo.	6 days	15 min.	15 min. anginal attacks	After occlusion: Absent Q_4; slurred R_4.	Alive
11	38	F	+	–	–	1½ days	2 min.	Asymptomatic	After occlusion: Elevated S-T_1, S-T_2 and S-T_3.	Alive
12	59	M	–	2 yr. on exertion	–	1 day	Angina at rest ± 15 min.	Angina 1+ 15 min. at rest.	After occlusion: Fused S-T all leads.	Dead (no autopsy)
13	60	F	–	–	4 mo.	2 wk.	Not known	Slight angina	After occlusion: i-v conduction defect; S-T fused in all leads. Absent Q_4.	Alive

TABLE I—CONT'D

14	53	M	–	1½ mo. with effort	–	Progressed gradually	20 min. angina at rest	Increased angina	Before premon.: Slurred R_2 and R_3; deep Q_3; T_4 slightly shallow. After premon.: No significant change.	Alive
15	69	M	–	4 wk. with effort	–	Progressed gradually	10 min. angina at rest	Increased angina	After occlusion: Left bundle-branch block.	Alive
16	45	M	–	–	3 wk.	1 wk.	½ hr.	Angina at rest	Before occlusion after premonitory: within normal limits—left axis dev. Died after occlusion. No electrocardiogram.	Dead (no autopsy)
17	64	F	–	–	4 yr.	1 wk.	5 hr.	Asymptomatic	Before premon. attack: Deep S_2, inverted T_3. After premon. attack: No significant change.	Dead (no autopsy)
18	58	M	+	–	–	4 days	20 min.	Asymptomatic	After occlusion: Left bundle-branch block.	Alive
19	63	M	+	–	–	1 wk.	2 hr.	Asymptomatic	After occlusion: Sl. inverted T-waves; S-T_1 elevated.	Alive
20	55	M	–	4 mo.	–	Progressed gradually	30 sec. more often than before	Anginal attacks as before	After occlusion: Elevated S-T intervals.	Alive
21	54	M	+	–	–	2 days	½ hr.	Asymptomatic	No electrocardiogram.	Dead (L. and R. occ.)
22	45	M	+	–	–	2 wk.	½ hr.	Recurrent angina ½ hr.	18 mo. before premon.: Deep S_2; diphasic T_4. After premon.: No significant change except in T_2 and T_4. After occlusion: Inverted T_1 and T_2; depressed T_4.	Alive
23	51	M	–	–	5 wk.	4 days	1 hr.	Asymptomatic	Before premon.: Prominent Q_1 and Q_2. High S-T_2; Q_4 present. Inverted T_4. After premon.: No change. After occlusion: No record.	Dead

TABLE I—CONT'D

CASE NO.	AGE	SEX	BEFORE PREMONITORY ATTACK			INTERVAL BETWEEN PREM. AND ACTUAL OCCLUSION	APPROXIMATE DURATION OF PREMONITORY ATTACK	CONDITION PREMONITORY BEFORE OCCLUSION	ELECTROCARDIOGRAMS	OUTCOME
			NO ANGINA	PROGRESSIVE ANGINA	ANGINA PECTORIS DURATION					
24	53	F	+	-	-	5 days	1½ hr.	Pulmonary edema after premon.; well after	After occlusion: Left axis deviation; T_1 flat; deep S_2.	Alive
25	65	M	-	-	2 yr.	1 day	1 hr.	Asymptomatic	Before premon.: Left axis deviation; $S\text{-}T_2$ and $S\text{-}T_3$ slightly elevated; T_1 flat. After occlusion: Slurred R_1 and R_4; absent Q_4; inverted T_2.	Alive
26	39	M	+	-	-	10 days	1 hr.	Anginal pain at rest 1 hr.	After premon.: Left bundle-branch block; T_1 inverted; T_4 upright. After occlusion: As above 2 wk.; T_1 isoelectric 2 mo.	Alive
27	65	F	+	-	-	2½ wk.	1 hr.	Asymptomatic	Before premon.: Left axis dev.; inverted T_3; diphasic T_4. After occlusion: Left bundle-branch block; deep Q_3.	Dead
28	51	M	+	-	-	2 days	40 min.	Asymptomatic	After premon.: S-T slightly depressed in Lead I and elevated in Lead III. After occlusion: Inverted T_2; absent Q_4; T_4 inverted.	Alive
29	54	M	+	-	-	2 wk.	20 min.	Asymptomatic	After occlusion: Left axis dev.; inverted T_1; low Q_{1a}; slurred R_1.	Dead (R. & L. ant. lesion)

averaged 7.1 days. During this period, of 16 patients who had not had previous anginal pain, only 2 had recurrent minor attacks. Of the remaining 14 patients, 2 had dyspnea, and the others were entirely asymptomatic. Most of these individuals not only were free from pain and dyspnea, but felt so nearly normal that it was difficult to enforce bed rest upon them. They were afebrile and had no changes in blood pressure. Such an individual was Patient 21, a fifty-four-year-old male, who had an attack of severe precordial pain lasting half an hour during an evening, and then returned to his heavy physical labor of pushing wheelbarrow loads of sand in road repair work. For the succeeding two days he did his work without distress in any form.

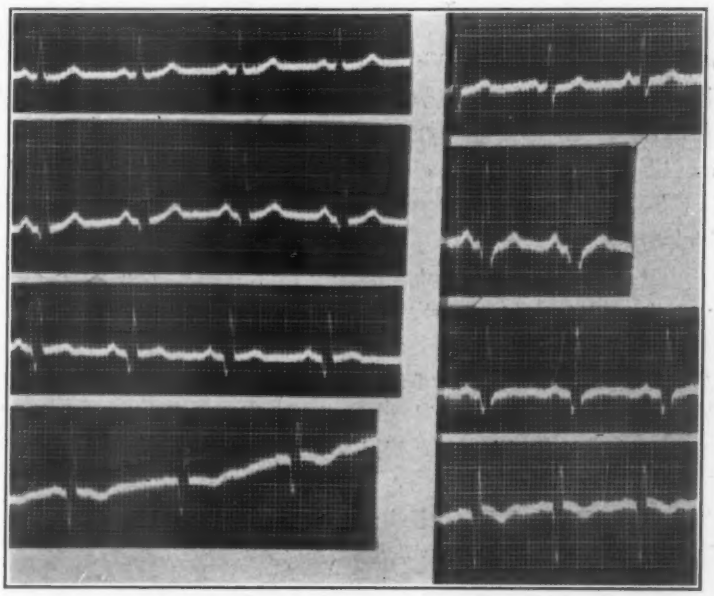

Fig. 3.—Mr. S. C. (Case 14). First record Feb. 13, 1936, ten days prior to premonitory pain of acute coronary artery occlusion. Second record, Feb. 24, 1936, one and one-half days after the premonitory pain but prior to the actual acute coronary artery occlusion. See legend of Fig. 1 for explanation of Leads IV *A* and IV *B*.

On the second night he experienced the pain and had the objective evidences of acute coronary occlusion, which proved fatal within forty-eight hours.

Patients 16 and 23 have been discussed previously relative to recurrent pain occurring prior to their fatal attacks.

The electrocardiograms taken were chiefly notable in that they offered no demonstrable assistance in making a diagnosis of impending thrombosis. Eight patients had electrocardiographic records taken in the interval between the premonitory and the final attacks; and of these, five had had previous records. In the tracings of these five

patients, no significant change was found after the heralding attack (Fig. 3). Of the records of the remaining three cases, one was normal; and one was not of diagnostic consequence because a coronary artery occlusion had occurred two years previously. Patient 26 presented the only instance of possible electrocardiographic changes prior to the occlusive attack. No previous record had been taken because this man was apparently well, and yet his electrocardiogram exhibited evidence of a left bundle-branch block (by recent terminology) when he was in the hospital during the premonitory period. The record changed very little during the two weeks after the occlusive attack but then gradually altered toward normal with less slurring of the QRS and isoelectric elevation of the inverted T_1. Such electrocardiographic alteration suggests that coronary artery changes had recently produced the original left bundle-branch block although, as stated, there is no positive evidence of the existence of this lesion prior to the origin of any cardiac symptoms.

As would be expected, the electrocardiograms of all patients having records taken after their occlusive attacks showed characteristic pathological changes.

Without taking into account histories of previous coronary occlusion, there was found to be a fatality of 34.5 per cent in the patients with the premonitory syndrome in our whole series of twenty-nine cases, as contrasted with a fatality of 50 per cent in the patients of the Mount Zion Hospital series who did not present the preocclusive picture. These figures are considerably higher than those presented by Conner and Holt,[4] who observed a mortality of 16.2 per cent in first attacks, and Master, Jaffe and Dack,[15] in whose series a mortality of 14 per cent for all attacks was found. Our small series includes all cases without relation to the number of attacks and the mortality corresponds more nearly with that of Levine's earlier group[16] in which there was a mortality of 53 per cent. The difference in fatality in the two groups mentioned here may be partially accounted for by the difficulty in obtaining a history of premonitory pain in those patients who were very ill when first observed, and in whom therefore the fatality rate obviously would be very high. Further explanation of the relatively lower mortality of patients with the warning syndrome is that when more gradual occlusion occurs, there is better opportunity for an effective collateral circulation to be established. Most observers of this entity have commented on the particularly grave outlook for the patient when severe shock suddenly develops early in the course of clinical arterial occlusion and on the more favorable prognosis of those patients in whom symptoms and signs develop more slowly. The preliminary stage described herein may well occur, however, only in

patients who under any circumstances would have a favorable outlook, either because small arterial branches are involved or for other reasons which are not known.

Only seven patients were kept in bed after the premonitory attack, and the fatality rate of this group was 29 per cent (two cases). This figure approximates the general fatality rate of the entire group, 34.5 per cent, and only study of a larger series of cases will answer the question as to whether bed rest may increase the chances of survival in such cases, when promptly diagnosed.

The diagnosis of the premonitory syndrome is made difficult because certain patients seem to present some of the characteristics mentioned previously but fail to develop the typical signs of a coronary artery occlusion within a period of weeks afterward. In patients with progressive angina pectoris, the attacks of pain may occur spontaneously and last for even an hour, with only transient relief from nitrite drug administration. In the event that these patients do not develop definitely the signs of coronary occlusion, one may predicate that either a silent small arterial block occurred or that the symptoms were really of no special significance.

In those individuals who have never had anginal pain, a severe attack of such pain may occur spontaneously without serious sequel. We have recently observed six such patients who were placed at complete rest, and within one to three weeks their attacks subsided and failed to recur after gradual convalescence. Whether this type of case represents an impending occlusion which was forestalled and in which collateral arterial supply was permitted to develop or whether it represents well-controlled ordinary angina pectoris is impossible to state.

SUMMARY AND CONCLUSIONS

Twenty-nine cases are presented exhibiting attacks of precordial pain of prolonged duration, which seem to represent a precursor phenomenon of characteristic acute coronary artery occlusion.

The nature of these attacks is discussed in relation to duration, distribution of pain, interval between the initial attack and the occlusion, association with previous history of angina pectoris, and eventual mortality.

The electrocardiograms in eight cases and the erythrocyte sedimentation rate in a single instance gave no indication of an active cardiac lesion or of the impending arterial occlusion.

The possible diagnostic importance of the impending occlusion with particular regard to outcome when complete bed rest is enforced was considered, but no conclusion was reached.

NOTE.—Since this paper was written, the work by Feil, mentioned previously as a personal communication, has been published (Preliminary Pain in Coronary Thrombosis, Am. J. M. Sc. 193: 42, 1937).

The publication of this work calls for certain brief comments. Feil estimated that 50 per cent of all cases of coronary thrombosis present preliminary pain without physical signs or other symptoms and this estimate is in close agreement with our figure. He states that the pain varied in duration from twelve hours to four weeks in the fifteen cases presented, but it is assumed that what is meant by duration was the interval between the first preliminary pain and the final complete occlusion. He comments on the spontaneity of the pain and the failure of nitrites to influence it, which factors we also have noted, but he fails to state the unusually long duration of the majority of individual attacks. He states that the electrocardiogram during the premonitory period may be normal or unchanged from records taken before the current illness. However, the records of three out of the five patients so studied exhibited abnormal forms or changes chiefly in the height and contour of the T-waves. We found only one instance of alteration of the electrocardiogram which probably took place during the premonitory period.

No comment is made by Feil on the existence of a difference in this pain in character or distribution from that of earlier attacks of true angina pectoris as was infrequently observed by us.

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THE WORK OF THE HYPERTHYROID HEART*

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THE majority of workers seem in agreement that no structural changes are characteristic of the "thyroid heart" as a result of the hyperthyroidism itself. Such changes as histiocyte infiltration, parenchymatous and fatty degeneration, fibrosis, and fraying of bundles which are commonly found in the heart of the hyperthyroid subject either accompany or follow other conditions also present which are damaging to the vascular system. Whatever increase in size occurs appears to be due to dilatation rather than to true hypertrophy.

While it appears to be generally admitted that whatever changes take place in the heart as the result of hyperthyroidism are functional, no clear-cut picture of these functional changes has yet been presented. A tachycardia is produced and, unlike that due to most agencies, is maintained long after isolation of the heart. It continues after removal of the sino-auricular node;[1] after crushing of the bundle of His;[1] and after complete denervation of the heart;[2] it appears in tissue cultures of embryonic chick hearts before any nervous elements are present, if the culture is subjected to the action of thyroxine.[3] Evidently the action of thyroid substance or of thyroxine is directly on cardiac musculature rather than upon nervous structures.

Evidence relative to the utilization of oxygen by the hyperthyroid heart is conflicting. Dock and Lewis,[4] using a heart-lung technique, conclude that the increased oxygen consumption of the hyperthyroid heart may be accounted for purely upon the basis of increased mass. McEachern,[5] by direct volumetric measurements upon the isolated hearts of thyroxinized guinea pigs, under conditions in which no appreciable work was done, found that such auricles utilized more oxygen than did the auricles of normal guinea pigs. McDonald[6] found that the hearts of terrapins heavily dosed with thyroid extract consumed more oxygen per gram of tissue than did the hearts of non-treated terrapins. These hearts appeared to pump a greater volume and to do more work than did the normal hearts, but no measurements were attempted to discover whether the hyperthyroid hearts really did more work. Clark and White[7] state that, provided no work is done, the rate of beat does not significantly influence the oxygen consumption of the auricles of cold-blooded animals.

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While increased work is generally admitted for the hyperthyroid heart, apparently little work has been done in demonstrating the actuality of such increase; no report of an attempt to analyze such increased work or to correlate it with oxygen consumption has been found. The study recorded below was planned in an effort to find whether increased oxygen consumption by the thyroid heart was represented in increased work. Because of the low glycogen content described for hyperthyroid hearts[8] and the somewhat uncertain state of our knowledge concerning the source of energy for the heart in pathological states,[9] I wished to observe the behavior of the hyperthyroid heart when subjected to a sudden strain such as is imposed upon it through treatment with epinephrine.

The method selected permitted me to measure rate of beat, amplitude, and volume output from which data I computed the work done by the heart under the various conditions imposed; it permitted me to measure the oxygen consumption and to correlate this function with the work done so far as correlation exists. The terrapin was the experimental animal used. Since animals in a previous study had shown evidence of extreme hyperthyroidism (grave muscular weakness, diarrhea, and emaciation) the treatment with thyroid substance was lessened in an effort to secure a degree of hyperthyroidism comparable to that commonly encountered clinically.

METHODS AND APPARATUS

Desiccated thyroid substance in suspension was administered by means of a stomach tube in dosage of 0.5 mg. per gram of body weight every eight days for a period of four weeks. The percentage of deaths among these animals did not differ from that of the control group. A definite tachycardia was noted in every case when the terrapins were opened.

The apparatus employed, similar to that previously described,[6] measured the oxygen required to resaturate at atmospheric pressure a previously saturated fluid after its passage through the isolated heart. Briefly, it consisted of: (a) A perfusion reservoir, a 150 c.c. Marriott flask which communicated by means of pure gum tubing and a glass "T" tube with a cannula inserted into the right precaval vein of the isolated heart (all other veins being ligated). The right-angle arm of this "T" tube was open and directed upward as a trap for any air bubbles that might enter the circulating system; (b) an oxygen chamber, a 50 c.c. Exax buret, cut off at 0.0 calibration and inverted into a 2.5 by 20 cm. sidearm test tube. The perfusion medium was pumped by the heart through a cannula inserted into the brachiocephalic artery (all other divisions of the aorta being ligated) through an "S" trap with a liquid seal into the oxygen chamber where it trickled through an atmosphere of pure oxygen down a thermometer suspended in the chamber; (c) an overflow reservoir identical with (a) from which the solution was pumped back to the perfusion reservoir by means of a 100 c.c. Luer type syringe and a 3-way glass stopcock. Each reservoir and the sidearm test tube were open to atmospheric pressure; (d) a light heart lever arranged to write upon a kymograph drum. This lever was weighted with 5 grams and attached by a thread and fine wire hook to the heart suspended by the two cannulas between the perfusion reservoir and the oxygen

chamber. In all records a downward excursion occurs during systole. During an experimental period the surface of the heart was kept constantly moistened by spraying or dropping Ringer's solution upon it.

The circulating medium in all experiments consisted of:

	PER CENT
Sodium chloride	0.650
Potassium chloride	0.014
Calcium chloride	0.012
Sodium bicarbonate	0.020
Sodium dihydrogen phosphate	0.001

This fluid was oxygenated by bubbling oxygen through it freely for a period of one hour. Because of marked changes which often occur in the response of the hyperthyroid terrapin heart some twenty to thirty minutes after administration of the drug, observations were made for a preliminary fifteen minutes to establish a normal for the particular heart, after which epinephrine-HCl was added to the perfusing fluid to the concentration of 1:500,000 and a second fifteen-minute observation made.

Oxygen consumption was read from the buret and reduced to standard conditions for temperature and barometric pressure; the volume pumped by the heart during each fifteen-minute period was measured with the calibrated syringe used to return the fluid to the perfusion reservoir; rate, amplitude, and variations in tone were obtained from the graphic records. On the expiration of an experimental period the heart was incised in all its chambers, blotted dry, and weighed. From the data secured was computed: the oxygen consumed per minute per gram of tissue; the work done in gm.-cm. per minute per gram of tissue; and, following the administration of epinephrine, the percentage increase in rate, amplitude, work done, and oxygen consumption. These data are set forth in averages in Tables I and II.

TABLE I

A COMPARISON OF THE BEHAVIOR OF THE NORMAL AND THE HYPERTHYROID HEART WITH RESPECT TO RATE, AMPLITUDE, WORK DONE, AND OXYGEN CONSUMPTION EXPRESSED IN AVERAGES

TYPE	RATE PER MIN.	AMPLITUDE CM.	WORK DONE PER GRAM TISSUE GM./CM./MIN.	OXYGEN CONSUMPTION PER GRAM TISSUE C.C./MIN.
Normal	31.1	2.2	140	0.026
Hyperthyroid	38.0	2.4	196	0.039

TABLE II

A COMPARISON OF THE RESPONSE TO EPINEPHRINE OF NORMAL AND HYPERTHYROID HEARTS WITH RESPECT TO RATE, AMPLITUDE, WORK DONE, AND OXYGEN CONSUMPTION EXPRESSED AS AVERAGES

TYPE	INITIAL	AFTER EPIN.	INITIAL	AFTER EPIN.
	Rate per minute		*Amplitude in cm.*	
Normal	31.1	42.8	2.2	2.65
Hyperthyroid	38.0	49.8	2.4	3.10
	Work done per gram tissue gm./cm./min.		*Oxygen consumption per gram tissue. cm./min.*	
Normal	140	233.4	0.026	0.033
Hyperthyroid	196	293.4	0.039	0.051

The volume pumped by each heart was noted but such wide variations appeared under comparable conditions that averages were rather meaningless. These variations

were due apparently to differences in auricular filling. In most hyperthyroid hearts ejection was quick and forcible; relaxation in many cases was prompt and auricular filling good. As a result of these facts increased rate was attended by a greater minute volume. In many cases, however, regardless of the nature of contraction, relaxation was much slower and the increased rate prevented good auricular filling between beats. In such cases the minute volume often fell markedly. We established our perfusion time at fifteen minutes because a majority of our hyperthyroid hearts showed a greatly decreased amplitude of beat some twenty to twenty-five minutes after treatment with epinephrine; unlike the normal hearts they do not respond to an increase in the concentration of epinephrine.

DISCUSSION

From this study the following salient facts seem to me worthy of consideration:

1. There is increased work per gram of tissue per minute done by the hyperthyroid heart. A definite tachycardia and a definite increase in amplitude combine to accomplish more work.

2. There is a greater consumption of oxygen per gram of tissue by the hyperthyroid heart as compared with the normal heart. A fair parallelism exists between the work done and the oxygen consumed by the two hearts. Whatever relationships may be shown finally to exist between oxygen consumption and work done by cardiac tissue, hearts exhibiting the degree of hyperthyroidism described for these animals succeed, under the conditions of excision and perfusion with Ringer's solution, in working close to the dynamic energy level of normal hearts under the same conditions. This work does not indicate the reason for the slightly greater oxygen consumption by the hyperthyroid hearts. Starling and Visscher[10] have shown that oxygen consumption by normal hearts is directly proportional to diastolic volume. Whether the hyperthyroid hearts used in this study underwent greater dilatation than did the normal hearts, or whether they possessed greater resting metabolism, or whether some unknown defect of contraction and recovery therefrom accounts for the slightly greater oxygen consumption are matters for further study.

3. Following the administration of epinephrine the normal and the hyperthyroid hearts show an average increase in rate of the same number of beats. The rhythmic apparatus of the heart is apparently uninjured through the action of the thyroid substance.

4. Both types of hearts show an increase in amplitude of contraction as a response to epinephrine. The increase shown by the hyperthyroid hearts is notably greater than that shown by the normal hearts. Furthermore, the increase in amplitude is achieved in a different manner by the two hearts. Normal hearts show greater systolic shortening and less diastolic relaxation. The lessened diastolic relaxation is in the

nature of increased tonus. The hyperthyroid hearts, however, show greater diastolic relaxation as well as greater systolic shortening as is demonstrated in Fig. 1. Approximately the same increase in work measured in gram per centimeter per minute per gram of tissue is accomplished by the normal and the hyperthyroid hearts in response to epinephrine.

5. The hyperthyroid hearts are able to maintain the additional work induced by epinephrine for a much shorter time than are the normal hearts. In from twenty to twenty-five minutes there is generally a marked falling off in amplitude without much, if any, change in rate. Further treatment with epinephrine does not call out renewed activity in these hearts as it does in the normal hearts.

6. The fair parallelism which existed between oxygen consumption and work done when we compare the hyperthyroid and the normal hearts under the conditions of excision and perfusion with a Ringer's

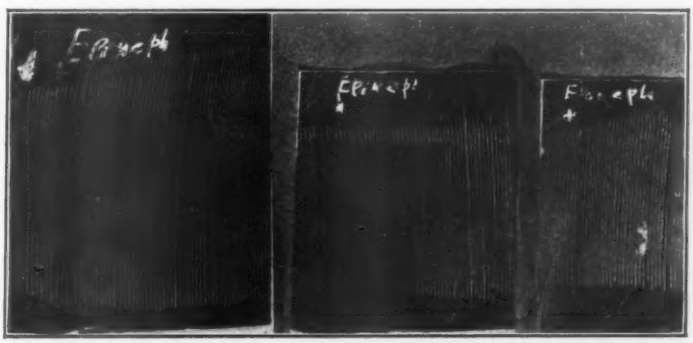

Fig. 1.—Showing the increased diastolic relaxation in the hyperthyroid heart following the administration of epinephrine. The upstroke occurs during diastole and the downstroke during systole.

solution disappears following the administration of epinephrine. The hyperthyroid heart uses much more oxygen and accomplishes, only for a little while, essentially the same additional work after which its work falls off rapidly. This observation is in harmony with that of Starling and Visscher[10] to the effect that the heart pushed to the level of its reserve utilized far more oxygen than when working at its normal level. Furthermore, the oxygen consumption which is unrepresented in work done under the conditions of our experiment is directly proportional to the degree of the hyperthyroidism present.

SUMMARY

In brief, may I say, this analysis of the work of the hyperthyroid heart indicates, I believe, that exhaustion of the cardiac reserve is the functional damage done to such hearts by hyperthyroidism and that the dilatation, far from being compensatory, is distinctly nonphysiological.

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THE DYNAMIC EFFECT OF ACUTE EXPERIMENTAL POISONING OF THE HEART WITH DIPHTHERIA TOXIN*

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AN ASSAY of the evidence in the literature leaves one in doubt as to the mechanism of action of diphtheria toxin on the circulation. There is evidence of peripheral circulatory failure, and there is evidence of cardiac failure, but which is primary is still a matter of controversy. The mere demonstration of a decreased blood volume (Harding[1]) and a drop of arterial blood pressure (Rolly,[2] Romberg and his coworkers[3]) does not preclude a cardiac origin for the diphtheritic circulatory collapse since it is well known that even acute coronary occlusion often leads to secondary circulatory failure. On the other hand, the demonstration of conduction disturbances (Stecher,[4] Marvin,[5] McCulloch,[6] Smith[7]), arrhythmias (Smith,[7] Shookhoff and Taran[8]), abnormalities in the contour of the electrocardiogram (Nathanson,[9] Marvin,[5] McCulloch[6]), and even the presence, post mortem, of degenerative changes in the muscle and interstitial exudations (Karsner,[10] Warthin[11]) does not necessarily mean primary cardiac failure. It is possible that such changes might follow peripheral circulatory failure, although this is not likely. This whole matter is of importance in dealing with the management of diphtheria poisoning because, in addition to specific therapy and the treatment of particular disturbances, the question comes up whether or not to institute supportive treatment for the heart. While the general practice recently has been in this direction, we felt that it might be worth while to investigate the actual dynamic changes following diphtheria poisoning.

The methods available made it necessary to use acute experiments. While, clinically, diphtheria is usually a protracted affair, fulminating acute poisoning does occur, and sudden death is not uncommon. We felt that our study would not only determine whether or not cardiac failure does occur, but would help to decide what relation the loss of cardiac power had to the conduction and rhythm disturbances with which the clinical studies have been primarily concerned. Such an analysis might help to decide, for example, whether or not heart failure, whatever its cause, always goes hand in hand with the electrocardiographic changes.

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METHOD

The study was based upon infusing a highly concentrated diphtheria toxin* (kindly supplied by Eli Lilly & Co. through the courtesy of Dr. K. K. Chen) intravenously over an average period of thirty-one minutes (range twenty-five to ninety minutes) into eighteen dogs anesthetized with morphine and sodium barbital.

The following variables were determined simultaneously in different combinations:

1. Heart rate (from various types of records).
2. Mean arterial pressure (from smoked drum records).
3. Venous pressure in the superior vena cava (with saline manometer).
4. Diastolic volume and stroke volume of the ventricles (from calibrated smoked drum records).
5. Systolic, diastolic and pulse pressures (and the contour of the pressure curves) in the right and left ventricles and in the aorta and pulmonary artery (with calibrated Wiggers' manometers). These records were recorded in pairs of various combinations.

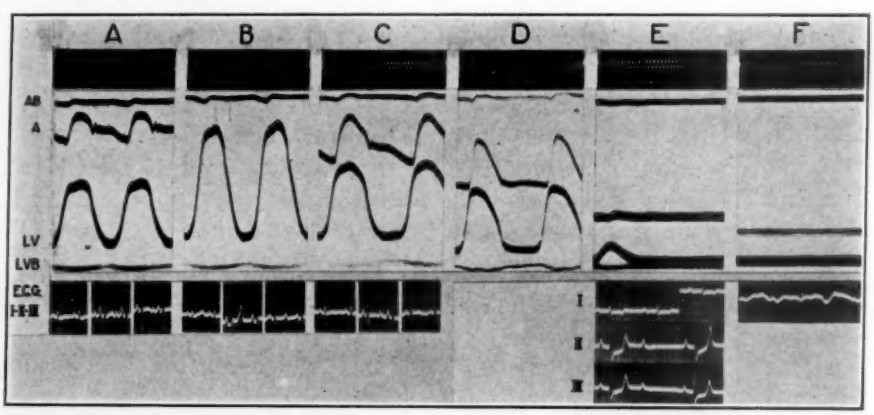

Fig. 1.—Series of curves to show the effect of diphtheria toxin on the aortic and left ventricular pressure curves and electrocardiogram. Time at top; each double vibration equal to 1/50 sec. *A* is aortic pressure curve; *LV* is left ventricular pressure curve. *AB* and *LVB* are base lines for the above. *ECG* is the three-lead limb electrocardiogram (time in 0.04 and 0.2 sec.). Segment *A* is control. *B*, taken during infusion of 50 c.c. of toxin. *C*, shortly after infusion. *D*, 5 minutes after *B*, during third injection of 50 c.c. of toxin. *E*, 6 minutes after *D*, 5 minutes after another 50 c.c. of toxin. *F* is ventricular fibrillation occurring soon after *E*. Discussion in text.

6. Changes in rhythm, in conduction in the heart, and in the contour of the standard limb lead electrocardiograms.
7. Changes in heart muscle tone from the ratio of diastolic size of the ventricles to their diastolic pressures (according to the principle recently outlined by Johnson and Katz[12]).
8. Asynchronism in the phase relations of the two ventricles (from their simultaneous optical pressure curves).
9. Minute volume of flow, calculated as the product of one-half the stroke volume and the heart rate.
10. The nature of the terminal fibrillation of the ventricles by means of high speed cinematography of the exposed heart which when projected gave slow motion. (In this, we were assisted by Mr. E. Sigman of this department.)

*L+ = 0.055 to 0.07 and an equivalent M.L.D. = 1/200 to 1/400.

DISCUSSION OF RESULTS

These changes were determined, tabulated, summarized, and then correlated. The chief findings are given briefly below. Typical records are shown in Figs. 1 and 2, and several consecutive frames of one cinematograph, in Fig. 3. The electrocardiographic findings are correlated in Table I.

The heart rate slowed in all experiments. This was due to a sinus bradycardia, usually with a sinus arrhythmia (Fig. 2, segment *E*),

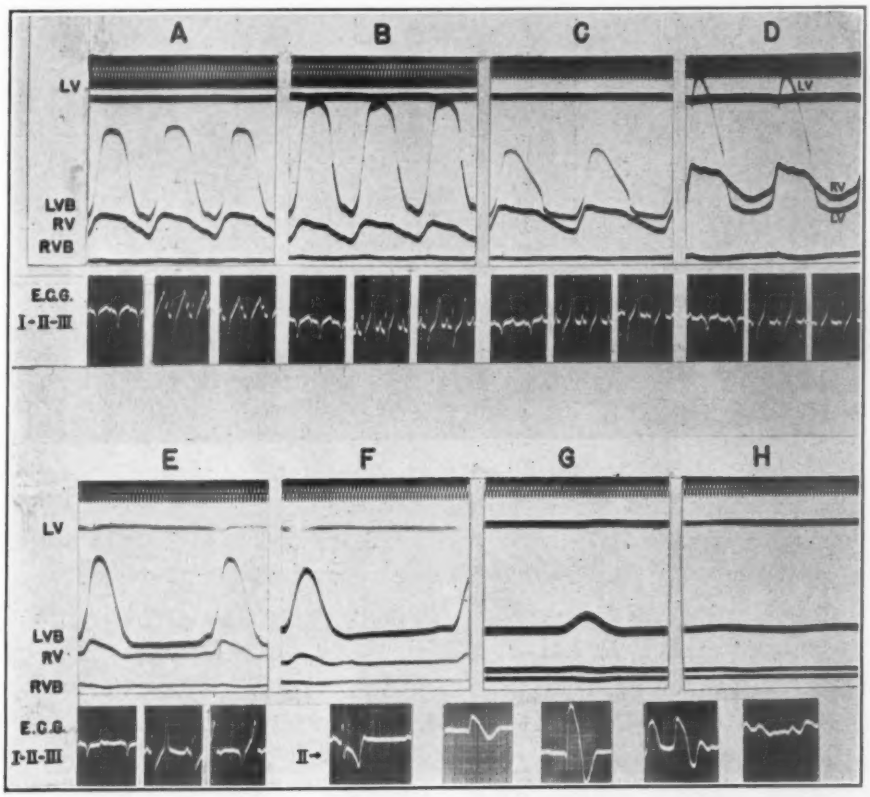

Fig. 2.—Series of curves to show the effect of diphtheria toxin on the left and right ventricular pressure curves. *RV* is right ventricular pressure curve and *RVB* its base line. Other conventions as in Fig. 1. Segment *A* is control. *B*, taken shortly after start of continuous injection of 50 c.c. of toxin. *C*, 5 minutes after *B*, during injection of second dose of toxin (50 c.c.). *D*, 4 minutes after *C*, during infusion of fifth 50 c.c. of toxin. *E*, 6 minutes after *D* and 1 minute after giving of ninth dose of 50 c.c. of toxin. *F*, 5 minutes after *E*, during injection of tenth 50 c.c. of toxin. *G*, 7 minutes after *F*, 5 minutes after eleventh 50 c.c. of toxin. *H* is terminal fibrillation occurring soon after *G*. Discussion in text.

or to an A-V block, either incomplete (Fig. 1, segment *E*) or complete. Apparently, the toxin acted both on the sinus node and on the A-V conducting system. In some instances the sinus slowing was extreme, and even the idioventricular rhythm was slower than usual. Our experiments do not reveal to what extent these changes might have

TABLE I

CORRELATION OF ELECTROCARDIOGRAPHIC DEVIATIONS FOLLOWING DIPHTHERIA TOXIN INJECTION

	EFFECT ON ELECTRO-CARDIO-GRAM	CAUSED DEPRES-SION OF S-T SEGMENT	CAUSED INVER-SION OF T-WAVE	CAUSED INTRAVEN-TRICULAR BLOCK	CAUSED PROLONGA-TION OF P-R INTERVAL	CAUSED HIGHER DEGREES OF A-V BLOCK	CAUSED APPEAR-ANCE OF PRE-MATURE SYSTOLES
1	N						+
2	P	+	+*	+	+	+	
3	P		+	+		+	
4	P			+			
5	P	+	+	+			
6	N						+
7	P		+*	+		+	+
8	P	+		+		+	
9	P	+		+	+	+	+
10	N						
11	P	+	+	+	+		
12	P		+		+	+	
13	N						
14	P	+	+*				
15	P	+	+*			+	
16	P			+		+	

*Toward end, T became positive again.
N, none.
P, produced a change.

been due to a vagus action, but there is no doubt that they were due to a large extent to a direct action on the cardiac conducting system, since intraventricular block occurred with a tremendous slowing of the invasion of the ventricles, at times the entire QRST complex becoming a smooth diphasic curve (Fig. 2, segment *G*). In five out of eighteen experiments, a preliminary acceleration was observed.

Premature systoles of various origins were frequently present, and it was not unusual to find them arising from multiple foci in a single experiment. Paroxysmal tachycardia, more often ventricular than auricular, also occurred, and "asystole" eventually resulted from standstill of the heart or, more frequently, from ventricular fibrillation. In most instances, this fibrillation was peculiar and different from the tumultuous fragmentary contractions seen in the ordinary type of fibrillation. As Fig. 3 shows, the heart was quiescent for the most part with ripples sweeping slowly over the ventricles. Probably this peculiar type of impulse-spread results from the markedly depressed conduction rate existing at this time. We have seen similar fibrillation on occasion following potassium or digitalis poisoning.

Usually before the conduction disturbances appeared, the contour of all the waves of the electrocardiogram changed (Figs. 1 and 2). Our results support the viewpoint expressed by Nathanson[9] that changes in electrocardiographic contour, when present, are an early sign of

diphtheritic myocardial poisoning. In four instances, however, terminal fibrillation of the ventricles occurred without any preceding alterations in the electrocardiogram.

The arterial blood pressure fell in both the systemic and pulmonary vessels, but this fall could not be related in time to any of the foregoing changes. At times a temporary preliminary rise in these pressures was seen, but was always associated with an increased minute volume output of the heart. It is impossible to determine from this study what the causal relationship is. The fall in pressure was due to vasodilatation since it occurred in three instances in spite of the

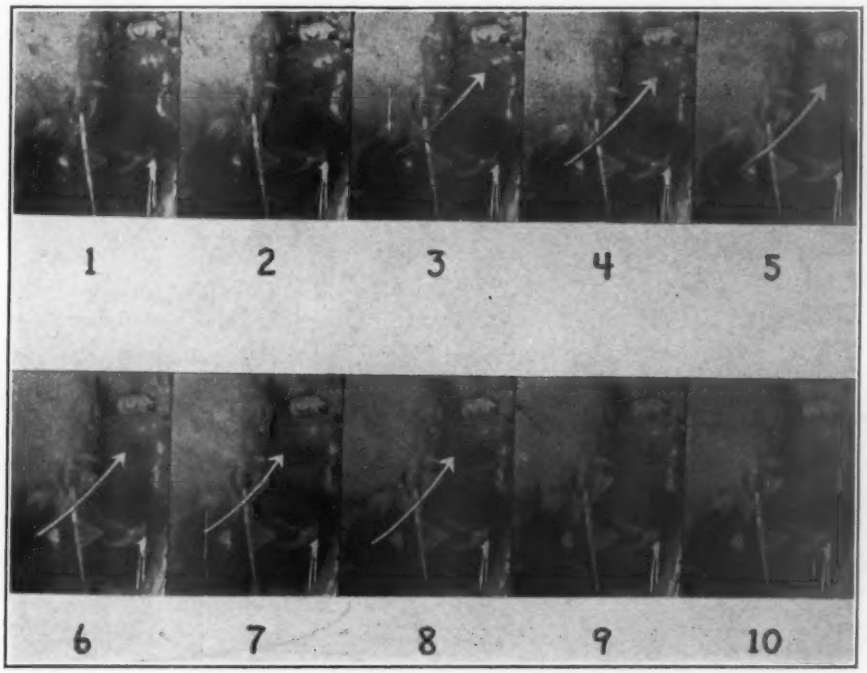

Fig. 3.—Ten successive frames from a cinematograph taken during typical terminal ventricular fibrillation which follows diphtheria poisoning. The white arrows indicate the rise and spread of one of the peculiar waves discussed in the text. Each frame represents 1/16 sec.

plethora and increased minute volume flow, and on four occasions preceded the decrease in minute volume output. In three other experiments the drop in pressure was contributed to by the decreased output of the heart. It follows that these vascular effects must be due in part at least to the direct action of the toxin.

The minute volume discharge of the heart increased at first, primarily as a result of the infusion, but later it declined despite the continued infusion. This may have been due, at times, partly to the poorer coronary blood flow which the drop in blood pressure could cause, but probably also to the depressing action of the toxin on the

contractile power of the heart. This is borne out by the fact that in three experiments, failure type of pressure curves were obtained with blood pressures at control levels and definitely above shock level. This occurred without any heart rate or electrocardiographic changes.

The stroke volume of the ventricles increased at first because of the infusion and later because of the slowing in heart rate; eventually the decrease in the contractile power of the heart overcame both the other factors so that the stroke volume declined. It is interesting to note that this decline in stroke volume occurred when the heart was distended and the initial pressure (the pressure existing before systole began) in its two ventricular chambers was still high—indicating real instances of overdistention, that is, distention that was detrimental to the heart and not beneficial as is true of the range in which Starling's law operates. This dilatation of the heart was not due to a plethora effect of the infusion since the quantities of fluid injected were too small, in four experiments being as little as 10 to 40 c.c. Distention was the direct result of the loss of power of the heart, permitting the accumulation of a systolic remainder in successive beats.

The pulse pressure in the aorta and pulmonary artery followed the changes in stroke volume except so far (a) as the dynamic effects were different in detail in the two ventricles in particular experiments and (b) as modified by changes in the distensibility of the arterial trees from time to time in the course of the experiment. The contour of these curves (Fig. 1) showed evidence, in the early stages, of the type of curves seen in a hyperdynamic heart working against high resistance and in the later stage, the smooth curves of the hypodynamic heart working against low resistance (Fig. 1, segment *D* and especially *E*). The evidence from these curves, therefore, jibes with the volume curve analysis. Further evidence for this view is found in the fact that despite the infusion, the distention of the heart, and the slowing, the duration of the ejection period of the ventricles, as well as their systoles, shortened in three out of six experiments measured. This is seen when the power of the heart is failing, as one of us has shown previously.[13, 14]

Similar changes in amplitude, contour, and span of the pressure curve were seen in the ventricular pressure recordings (Fig. 2). Here it can be seen that the infusion (with its resulting distention of the heart) and the slowing (with the greater resulting filling time) at first tend to make the ventricles more powerful parallel with the elevation in the diastolic pressure levels (segments *A*, *B* and *D*). Later, however, despite these influences, the curves became smaller in height, shorter in duration, and smooth. This failure type of curve was associated in Fig. 2, and in the other experiment having records of

both ventricles, with a drop in the diastolic levels. (In Fig. 2 compare segment *D* with *E, F,* and *G* and segment *A* with *C*.) This occurred in both chambers while the ventricles continued to increase in volume as apparent to the eye. This can only mean a loss of tone. Decreases in diastolic pressure occurred in a single ventricle in other experiments but no record was obtained of both ventricles except in the above two experiments. These observations are in accord with those of Johnson and Katz[12] that loss of tone occurs in the heart whose power is failing. It is further evidence of loss of power and is partly responsible for establishing the vicious cycle of overdistention.

The late drop in diastolic pressure within the right ventricle may account for the secondary decline in venous pressure seen toward the end of three of these experiments, although the venous pressure drop may also be due to a decrease in the return of blood to the heart because of stasis in the periphery.

Examination of our curves showed that events in the two sides of the heart were not always in phase; at times they went in opposite directions (segments *A* and *B* of Fig. 2). This phenomenon we have previously discussed (Brams and Katz[15] and Johnson and Katz[12]); it indicates the independence between the right and left hearts. We have found again, as previously stated (Katz[16]), that the start of systole and ejection is not synchronous in the two ventricles. Further, we noted that in one experiment the changes in this asynchrony of systole were decidedly smaller than the change found in intraventricular conduction time. This observation dealing with asynchrony is opposed to the view that intraventricular block is confined to one or the other ventricle and favors the contrary view that the block is often equally severe in both ventricles.

There is no doubt that the peripheral actions of the diphtheria toxin contributed to the failure of the heart in these experiments just as failure of the heart contributed to the peripheral vasodilatation and stasis. Nor is there any doubt that the action of the diphtheria toxin on conduction contributed to the heart failure. Nevertheless, we found evidence that the action of the toxin on the power of the heart often preceded the other cardiac actions and the peripheral effects. This is well shown by the curves in Fig. 2 (segments *B, C, D, E* and *F*).

It is of practical clinical importance to realize that diphtheria toxin acts directly on the contractile power of the heart and its tone since serious damage to the heart may be present without significant modification of the electrocardiogram or of blood pressure. Histological examination of these hearts failed to reveal any changes other than cloudy swelling. (We are indebted to Dr. O. Saphir of the Department of Pathology for this interpretation.)

SUMMARY

The acute effect upon the cardiac dynamics of injecting diphtheria toxin was studied in dogs. The study was based on records of mean arterial and venous blood pressures and records of the volume and pressure changes of the heart. Electrocardiograms were obtained also. The pressure curves of the various heart chambers (i.e., the two ventricles, the pulmonary artery, and the aorta) were recorded with Wiggers' manometers on a photokymograph. The volume and mean pressure curves were obtained on a smoked drum.

It was found that the diphtheria toxin produced a sinus slowing of the heart and, later, various types of A-V and intraventricular block. Extrasystoles of various types and paroxysmal tachycardia also were present, and eventually the heart went into a peculiar type of ventricular fibrillation which we have described. A vasodilatation in both the systemic and pulmonary circuits also resulted. Heart failure was caused by these disturbances in conduction and rhythm, and by the decreased coronary blood supply following systemic vasodilatation. There was definite evidence, however, that diphtheria toxin poisoned the heart in such a way that myocardial failure with its typical abbreviated and less powerful contraction occurred sometimes before these other changes came into operation. There was evidence also of a loss of tone in the ventricles toward the end. It is of practical importance to realize that diphtheria toxin acts directly on the contractile power and tone of the heart since serious damage to the heart may be present or develop quickly before significant modification of the electrocardiogram or of blood pressure is present.

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MIDAXILLARY LEADS OF THE ELECTROCARDIOGRAM IN MYOCARDIAL INFARCTION*†

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THE midaxillary or lateral thoracic leads of the electrocardiogram, in some cases, appear to show earlier and to a more marked degree than the limb leads, the electrocardiographic changes characteristic of infarction in the part of the left ventricle supplied by the left coronary artery, and there is a suggestion that these changes may sometimes last longer than they do in the limb leads. On this account this work is presented, the writer hoping that others with greater facilities at their command may be able to report further clinical, and especially further post-mortem, data on this subject.

A proper understanding of this subject necessitates a review of the development of our present knowledge of the electrocardiographic localization of myocardial infarction, for it is on the previous work on this subject that the greater part of the present study is based.

Barnes and the writer[2] showed that changes in the RS-T segment and T-wave in the limb leads of the electrocardiogram often give indication of the part of the heart involved in myocardial infarction. We showed that, for the most part, infarction is generally confined to the left ventricle. Our work indicated that infarction of the part of the left ventricle usually supplied by the left coronary artery (that is, the anterior portion of the left ventricle and the anterior part of interventricular septum which are generally supplied by the anterior descending branch of the left coronary artery and sometimes the left, or obtuse, margin and left part of the posterior basal portion of the left ventricle where supplied usually by the circumflex branch of the left coronary artery) generally caused the so-called T_1 changes to occur in the electrocardiogram. In this paper, in order to avoid repetition, this type of infarction will be called a T_1 type of infarct. We found these T_1 changes in the electrocardiogram to consist of an early elevation (elevation not always seen) of the RS-T segment in Lead I alone or Leads I and II combined. This was followed by an inversion of the T and often by a depression of the RS-T below the isoelectric line in Lead I alone or Leads I and II combined. We also observed that similar changes in the RS-T and T, except that they occurred in Leads II and III, the so-called T_3 type of electrocardiogram, generally were associated with infarction in the posterior part of the interven-

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†A preliminary report of this work was presented at the annual meeting of the Texas State Heart Association, Houston, Texas, May 25, 1936.

tricular septum and the adjacent portion of the posterior basal part of the left ventricle which usually is supplied by the right coronary artery. In this paper, for the sake of brevity, infarction in this location will be called a T_3 infarct.

Our work on localization of myocardial infarction has been confirmed by numerous writers. In addition, it has been added to as a result of the work on the Q-wave by Pardee,[7] Fenichel and Kugell,[3] and Wilson and his associates,[12] so that now it is generally accepted that a large Q_1 may be a part of the picture of the T_1 type of infarction and a large Q_3 may be associated with the T_3 type, with certain other requirements.

It was soon recognized that infarction produced by a left coronary artery lesion was not as readily shown by the electrocardiogram as that usually resulting from a right coronary artery lesion. The T_1 changes made their appearance later and sometimes were not observed at all. Wolferth and Wood[13, 14] called attention to this and introduced the anteroposterior thoracic leads, which they called Leads IV and V. With the use of these new leads they were able earlier to recognize infarction produced in the part of the heart generally supplied by the left coronary artery, and at times they could demonstrate it when it did not register at all in the limb leads. They considered the early findings of this lesion to be a depression of the RS-T_4 and a deep inversion of T_4. Later Q_4 usually disappeared, T_4 became upright and RS-T_4 might become slightly elevated. Changes in Lead V were reported as similar to those in Lead IV. The T_3 type of infarct (usually from a right coronary artery lesion) did not appear to be as well shown in the anteroposterior leads as in the standard limb leads.

Why does not the electrocardiogram register a T_1 type of infarct (left coronary artery lesion) as well as a T_3 type (right coronary artery lesion in most hearts) in the standard limb leads? If we consider the pathway that the electrical current is most likely to follow in the three limb leads one possible explanation suggests itself. In Lead I, with the right arm electrode applied to the right arm and the left arm electrode attached to the left arm, the shortest pathway for the electric current to pass would be from the right arm through the right shoulder region to the left shoulder and left arm. This is entirely above the heart. Wilson,[12] and Wolferth and Wood[13] have stated that the nearer an electrode is to the infarct the more likely it is to register the infarct and, conversely, the farther away it is the more indifferent the electrode becomes. If this be true, then Lead I is more indifferent than Leads II and III, as it is farther away from the left ventricle or even the heart itself. For Lead I to be made more sensitive to T_1 changes it would have to be taken so that the shortest path for the current to travel would run nearer to, or even better, directly through the heart itself. Following out this line of reasoning, the right arm

electrode was placed in the right midaxillary line and the left arm electrode in the left midaxillary line and the left leg electrode was applied to the left leg in its accustomed place. The regulation large metal electrodes were used and the electrodes were applied in such a manner that the long axis of the electrode rested on the midaxillary line (Fig. 1). Three midaxillary leads were taken. The first midaxillary lead (ax_1) was from the right midaxillary line to the left midaxillary line and was taken by setting the electrocardiograph as in taking Lead I of the limb leads. The midaxillary Lead II (ax_2) was taken by setting the electrocardiograph to take Lead II, the current passing from the right midaxillary line to the left leg. The midaxillary Lead III (ax_3) was taken by setting the electrocardiograph for Lead

Fig. 1.—Left lateral view showing the left arm electrode in place in the left midaxillary line. The right arm electrode was similarly placed in the right midaxillary line.

III and the direction of the current was from the left midaxillary line to the left leg. The first tracing using the midaxillary leads was taken Sept. 18, 1934 (Fig. 3).

Although it is natural to suspect that lateral thoracic leads should be investigated following the valuable contributions of Wolferth and Wood[13] on anteroposterior thoracic leads, the writer has found no published record of them. However, on May 12, 1936, Lundy[6] stated to the writer that in some unpublished work he had made 1,000 tracings, using the midaxillary Lead I (Lundy calls this Lead SS, meaning side to side). It is possible that he began his work first. However, his approach to the subject differs from the study here presented. Groedel[4] used a lead in which the right arm electrode was placed on

the right arm and the left arm electrode was placed in the left anterior axillary line at the level of the lower end of the sternum, which he considered to be especially sensitive for the left ventricle. Groedel's lead does appear to be quite sensitive to T_1 electrocardiographic changes, but does not register them quite as markedly as the midaxillary Lead I, as is seen later in this paper. Hyman[5] has been working with various thoracic leads but his work is as yet unpublished.

Since Sept. 18, 1934, the midaxillary leads have been used on more than 600 cases. Of this number there were many normal cases, some of which were studied for control purposes and others in the course of routine examinations. The normal (Fig. 2) for the midaxillary Leads I and II was the same as for the corresponding limb leads except that the voltage was a little greater in the midaxillary leads. In

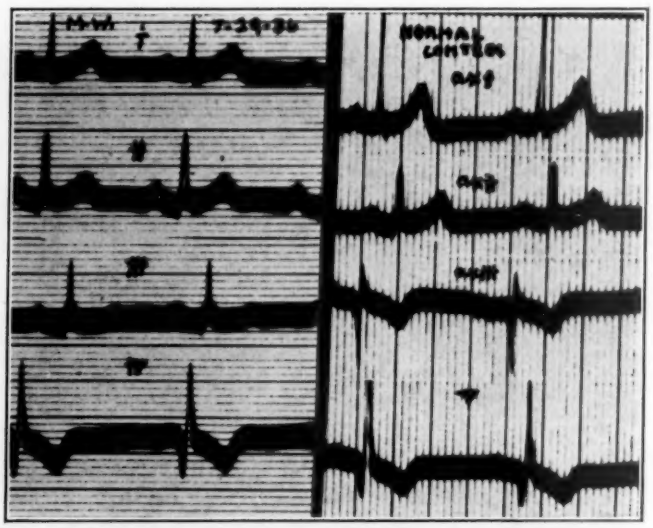

Fig. 2.—A normal control electrocardiogram. The complexes of the midaxillary leads are similar to those of the standard limb leads. Leads one to five are indicated in small Roman numerals, i, ii, iii, iv, and v, in this and the following figures. The midaxillary leads are marked ax_I, ax_{II}, and ax_{III}.

no case was there any inversion of the T-wave or isoelectric T or diphasic T in midaxillary Lead I alone or the combined Leads I and II unless there was definite clinical evidence to account for it. The same applied to abnormalities of the RS-T segment and the Q-wave. On the other hand, whenever the T-wave was inverted in the limb Leads I or I and II it was always found to be inverted in the corresponding midaxillary leads.

Midaxillary leads have been studied in 38 cases with definite history and electrocardiographic findings of myocardial infarction. Cases with bundle-branch block were not included. The three conventional leads and Leads IV and V* also have been taken for comparison. In some

*The anterior electrode was placed just to the left of the sternum and not at the apex for Leads IV and V.

only one tracing has been taken and in others it was possible to obtain serial electrocardiograms. In order to conserve space the history and electrocardiograms of all of these cases will not be presented. However, typical cases will follow to illustrate better the findings in this study.

There were 18 cases in this group with the T_1 type of electrocardiographic changes. Cases 1, 2, and 3 are of that type.

CASE 1.—Mr. D. S. was seventy-nine years old in July, 1933, when he began having anginal attacks. On Sept. 15, 1934, he had a severe acute myocardial infarction with pain lasting twenty hours. Pulmonary edema soon followed. He had another attack of pain Sept. 21, 1934. His death occurred Oct. 18, 1934. There was no post-mortem examination. An electrocardiogram on Sept. 17, 1934, showed a deep Q_1, a high

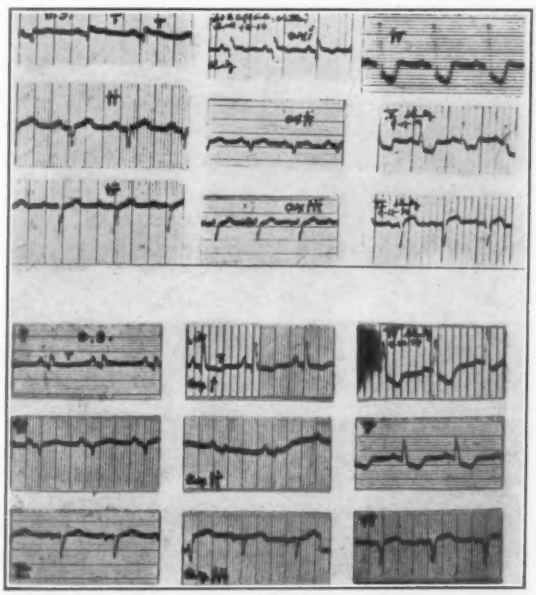

Fig. 3.

Fig. 4.

Fig. 3.—Case 1. Electrocardiogram three days after onset of acute myocardial infarction. Elevation of RS-T_1. Depression of RS-T_4 and RS-T_5. Deep Q_1 and midaxillary Q_1. T_1 is positive but the midaxillary T_1 has already become inverted.

Fig. 4.—Case 1. Electrocardiogram seven days after onset of myocardial infarction. T_1 has now become inverted but not as deeply as the midaxillary T_1. Midaxillary T_2 has become flattened.

take-off and definitely elevated RS-T_1, an inverted T_1, a complete absence of Q_1 and Q_3 and a marked depression of RS-T_4 and RS-T_5. On the following day, and just seventy-two hours after the onset of the pain, the first experiment with the midaxillary leads was performed. The tracing at this time was similar to the one of the previous day so far as the conventional leads and the anteroposterior leads were concerned, except that T_1 was not inverted (Fig. 3). In the midaxillary Lead I, Q_1 was greater than the limb Q_1 and midaxillary T_1 was inverted. On Sept. 20, 1934, a tracing was essentially the same except that T_1 of the limb leads had become slightly inverted and in the midaxillary Lead I the T had become more deeply inverted. In the limb leads T_2 was upright but in the midaxillary leads it was lower and somewhat diphasic. The last electrocardiogram, taken on Sept. 22, 1934, showed no further change (Fig. 4). In this case the T_1 type of change had been found to

be a little more marked in the midaxillary Leads I and II than in the corresponding limb leads. Furthermore, it appeared that these changes were a little further advanced in the midaxillary leads, suggesting that the proximity of the path of the lead to the heart had something to do with the form of its waves. It was because

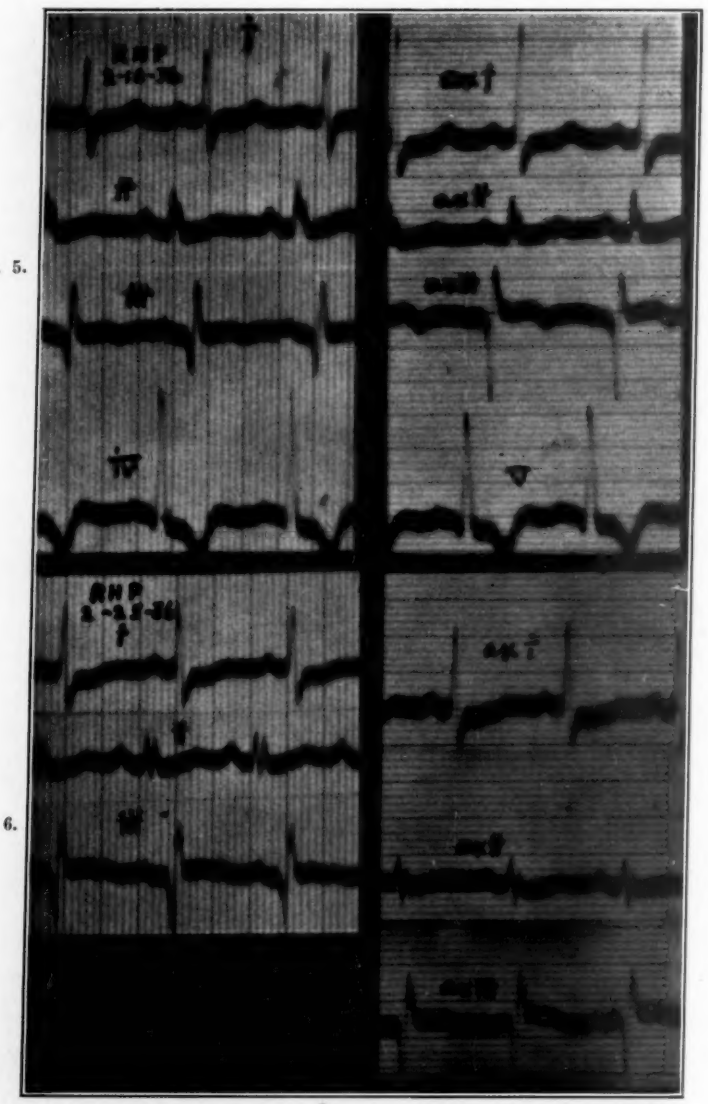

Fig. 5.

Fig. 6.

Fig. 5.—Case 2. Electrocardiogram on Feb. 10, 1936. Severe anginal attacks were experienced previous to this electrocardiogram but the acute myocardial infarction came later. The electrocardiogram was similar on Dec. 26, 1935.

Fig. 6.—Case 2. Electrocardiogram Feb. 25, 1936, taken fifteen hours after onset of acute myocardial infarction. The electrocardiogram was similar eight hours later. Note the depressed RS-T segment and diphasic T_1 in the limb and midaxillary leads. Q_4 has become normal.

the T_1 changes in the midaxillary leads seemed further advanced than in the limb leads in this case that additional cases were studied.

CASE 2.—Mr. R. H. P. was forty-eight years of age when first seen Feb. 25, 1931. He weighed 230 pounds. His electrocardiogram was normal at that time and on April 17, 1934. His blood pressure was 128 mm. of mercury systolic and 90 mm. diastolic. In the fall of 1935 when he was rejected for life insurance his blood pressure was 150 mm. of mercury systolic and 110 mm. diastolic. He had had anginal pains for a number of months and on Dec. 25, 1935, he had a severe attack lasting about one hour. The electrocardiogram on the following day was similar to Fig. 5, showing a deep Q_3 in the limb and midaxillary leads and a small Q_4 and Q_5. The QRS_2 was notched in the limb and midaxillary leads. He had another attack Feb. 9, 1936, and on the following day the electrocardiogram showed no further changes. On Feb. 24, 1936, he developed severe substernal pain which lasted twenty-four hours and was not relieved completely by hypodermic administration of morphine or dilaudid. An electrocardiogram taken fifteen hours after the onset of this attack showed a depression of the RS-T_1 and a diphasic T_1 in the limb and midaxillary leads. Lead IV was normal and remained so, as did Lead V in all of the remain-

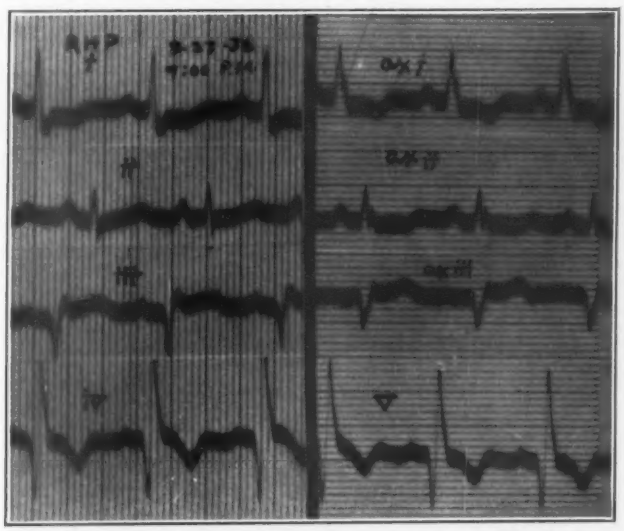

Fig. 7.—Case 2. Electrocardiogram of Feb. 27, 1936, taken three days after onset of infarction of myocardium. T_1 is still diphasic in the limb leads but has become inverted in the midaxillary Lead I and somewhat diphasic in the midaxillary Lead II. Leads IV and V are normal.

ing tracings (Fig. 6). The electrocardiogram was similar twenty-three hours later. Two electrocardiograms taken on Feb. 28, 1936 (Fig. 7), showed no further change in the limb Lead I, but in the midaxillary Lead I the T was definitely inverted. Tracings on March 4 and 5, 1936 (Fig. 8), showed inverted T_1 in both the limb and midaxillary leads. The T_1 inversion and RS-T_1 depression and upward convexity were much greater in the midaxillary Lead I than in the corresponding limb lead. Midaxillary T_2 was diphasic, while the conventional T_2 was upright and unchanged. On March 27, 1936, T_1 was isoelectric, while the midaxillary T_1 was still deeply inverted and the midaxillary T_2 diphasic (Fig. 9). On May 2, 1936, and on June 5, 1936 (Fig. 10), the entire electrocardiogram was normal except that the midaxillary T_1 was diphasic and the RS-T in that lead was slightly depressed. On July 13, 1936, T ax_1 was positive. The only reminder of the accident was a low take-off of the RS-T in Lead I and a still lower take-off in midaxillary Lead I.

The serial electrocardiograms in this case have shown the characteristic electrocardiographic changes following myocardial infarction of the T_1 type to appear earlier, to be more marked, and to last longer in the midaxillary than in the limb leads. In two tracings (Fig. 8)

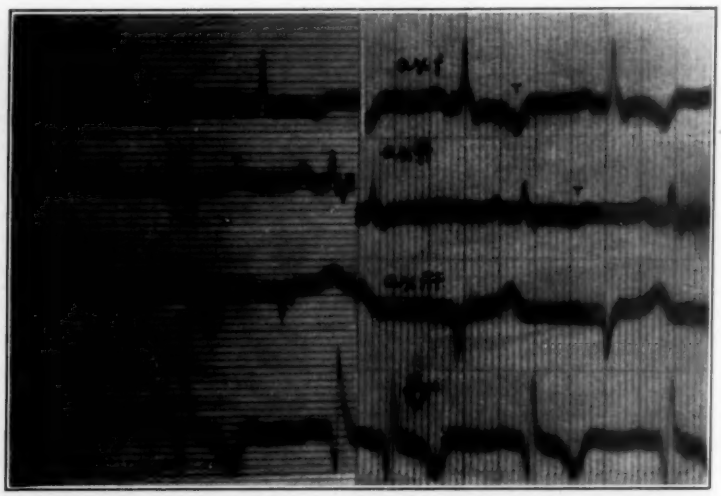

Fig. 8.—Case 2. Electrocardiogram taken March 5, 1936. T_1 is inverted in the limb and midaxillary leads, but the T_1 inversion and upward convexity of the RS-T segment are much greater in the midaxillary lead. T_2 is upright in the limb lead, but diphasic in the corresponding midaxillary lead.

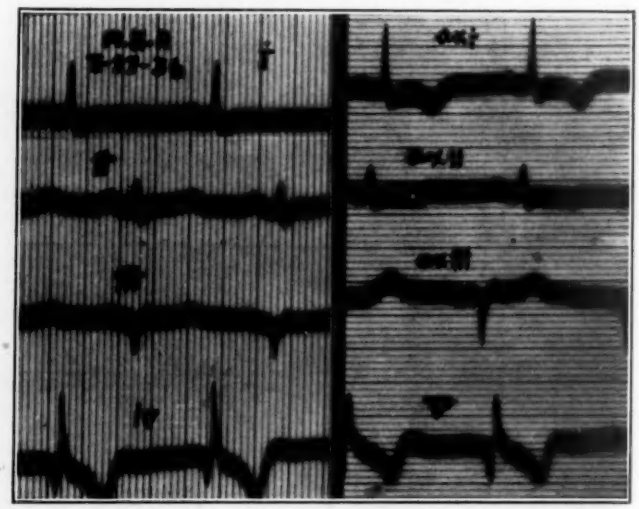

Fig. 9.—Case 2. Electrocardiogram taken March 27, 1936, thirty-one days after onset of myocardial infarction. The limb lead T_1 is now isoelectric, while in the midaxillary leads the T_1 is still deeply inverted and the RS-T_1 still has a definite upward convexity and T_2 is still diphasic.

definite inversion of the limb T_1 did occur to show that this was really a T_1 type of infarct. Leads IV and V of Wolferth and Wood,[13] though abnormal previously, remained normal after the onset of the infarction.

CASE 3.—Mr. I. R. I., aged forty-eight years, was seen in a neighboring city July 27, 1935, and an electrocardiogram was taken at that time. Three days previously he had begun with a typical history and later had the usual laboratory findings of acute myocardial infarction. The electrocardiogram showed a low voltage except

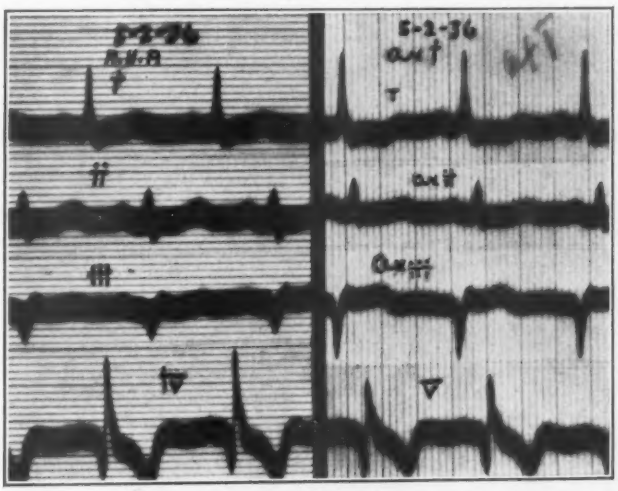

Fig. 10.—Case 2. Electrocardiogram taken on May 2, 1936. The T is now positive in the limb Lead I (i) but is diphasic in the midaxillary Lead I (ax_1) and the RS-T segment is still depressed below the isoelectric line in the latter lead.

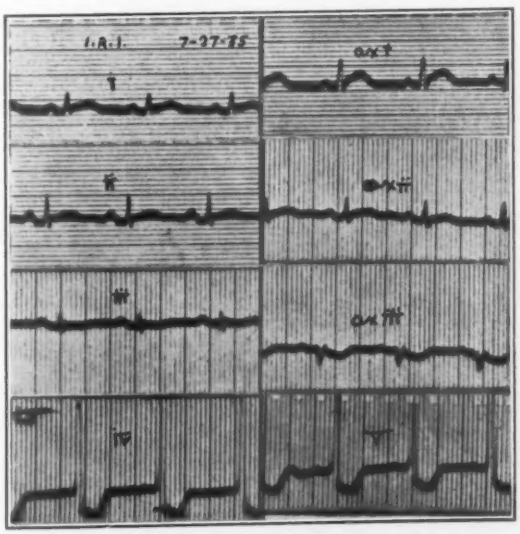

Fig. 11.—Case 3. T_1 type of electrocardiogram three days after onset of myocardial infarction. The elevation of the RS-T shows better in the midaxillary Lead I (ax_1) than in the corresponding limb lead (i). Depressed RS-T_4 and RS-T_5.

in Leads IV and V (Fig. 11). The only evidence of a recent infarction registered in the limb leads was a scarcely recognizable elevation of RS-T_1. The RS-T in the midaxillary Lead I was more definitely elevated and ended in an upright T. The amplitude of the QRS in the midaxillary Lead I was greater than in the correspond

ing limb lead. Q_4 and Q_5 were absent and RS-T_4 and RS-T_5 were depressed. This is a typical early T_1 type of electrocardiogram with the changes more marked in the midaxillary and the anteroposterior thoracic leads than in the limb leads at the time the tracing was taken.

Besides the 3 cases briefly presented, 15 additional cases of the T_1 type were studied, making a total of 18 in all. Data concerning all 18 cases may be found in Table I. In 15 of these 18 cases the changes in the T-wave were more marked in the midaxillary T_1 than in the limb T_1. In the remaining 3 cases the T-changes were practically equal in the limb and midaxillary leads. In 6 cases it was shown that the T changes had occurred earlier in the midaxillary T_1 than in the limb T_1. In the remaining cases the electrocardiograms were not taken early enough or often enough to see in which the change occurred earliest, the limb or midaxillary leads. In no case was the T_1 change more marked or seen earlier in the limb than in the midaxillary leads. In 2 cases in which it was possible to follow through with serial electrocardiograms the T_1 changes persisted longer in the midaxillary Lead I than in the limb T_1. In no case was the reverse true. Because of persistent electrocardiographic changes, inability to secure serial electrocardiograms, and fatalities, the duration of the persistence of the T abnormality is unknown in most of the cases.

TABLE I

SUMMARY OF T_1 CASES. A COMPARISON OF THE CHANGES IN T_1 AND T_2 IN THE LIMB AND MIDAXILLARY LEADS

CASE	T_1 CHANGES MORE MARKED*	T_1 CHANGES APPEARED EARLIER†	T_1 CHANGES PERSISTED LONGER‡
1	ax_{1-2}§	ax_{1-2}	ax_2
3	ax_1		
2	ax_{1-2}§	ax_{1-2}	ax_{1-2}
4	ax_2		
5	ax_1		
6	ax_1		
7	ax_1	ax_1	
8	ax_1		
9	equal‖		
10	ax_{1-2}	ax_{1-2}	
11	equal		
12	ax_1		equal
13	ax_{1-2}	ax_2	
14	ax_1		ax_1
15	ax_1		
16	ax_1		
17	ax_1	ax_1	
38	ax_1	ax_1	

*Where ax_2 has been omitted it was normal or the changes were equal to those of the limb T_2.

†Where nothing has been recorded the electrocardiogram was not taken early enough to determine if changes appeared earliest in limb or axillary leads.

‡Where nothing has been recorded the patient was not followed long enough to determine if the electrocardiographic changes persisted longer in the midaxillary than in the limb leads.

§Limb T_2 never was abnormal.

‖T_1 changes were transient in both limb and midaxillary leads and quickly disappeared.

Changes in Lead II in this series of T_1 type infarcts were found to be more marked in the midaxillary position than in the limb leads in 5 of 16 cases in which this lead was taken. In 3 of these 5 cases the limb Lead II was normal. The limb Lead II changes in no case were greater than the midaxillary Lead II changes but were equal in 6 of the 16 cases. Lead II changes lasted longer in 2 cases in the midaxillary leads, but in no instance did the limb Lead II changes persist longer than those in the midaxillary Lead II.

The T_1 changes which were observed in the midaxillary Leads I and II in the cases in this group included significant elevation or depression of the RS-T segment, inversion of the T, cove-shaped (coronary) RS-T segments, and Q-waves of increased amplitude. Naturally all of these changes were not necessarily present in any one given case.

There were 14 cases showing a T_3 type of tracing included in this series. A brief description of 2 cases follows.

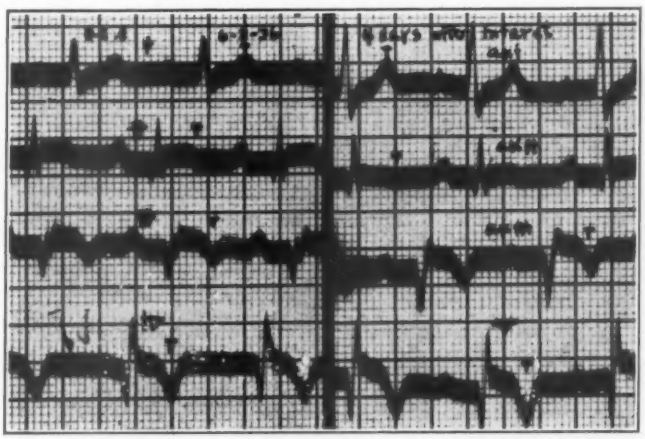

Fig. 12.—Case 18. Early T_3 type of electrocardiogram taken four days after the onset of acute myocardial infarction and showing elevated RS-T in the limb and midaxillary Leads II and III and in Leads IV and V. Also showing diphasic T_2 and inverted T_3 in the limb and midaxillary leads. The T_3 changes are slightly more marked in the limb than in the midaxillary leads.

CASE 18.—Mr. O. C., aged forty-six years, had an acute attack of myocardial infarction four days before the electrocardiogram was taken. The tracing (Fig. 12) showed a diphasic T_2 in the limb and midaxillary and anterior axillary leads* and an inverted T_3 in the limb, anterior axillary and midaxillary leads. The RS-T was elevated in Leads II, III, IV, V, ax_2, anterior ax_2 and anterior ax_3. There was a deep Q_2 in the limb leads and a deep Q_3 in the limb, anterior axillary and midaxillary leads. The changes in Lead II were a little more prominent in the limb leads than in either of the axillary positions.

CASE 19.—Mr. T. B. R., aged forty-nine years, was seen by me for an electrocardiographic study only. He had had angina pectoris during the preceding six

*In the anterior axillary leads the right arm electrode was placed on the right anterior axillary line and the left arm electrode on the left anterior axillary line, instead of in the corresponding midaxillary positions. This generally gave waves directed in the same direction but of greater amplitude than midaxillary leads in Leads I and II.

months. Acute myocardial infarction had begun about fifty-two hours before the tracing was taken and the pain had continued up to that time except when he was under the influence of morphine. The electrocardiogram (Fig. 13) showed a normal T_1 in the limb leads. In Leads II and III the RS-T was elevated markedly, with a high take-off from a notched R-wave. Large Q_2 and Q_3 were also present. In the midaxillary Lead I the T-wave was practically isoelectric and if there was any deflection from the isoelectric line it was toward inversion of the T. There was also a small Q in midaxillary Lead I. Midaxillary II was almost identical with Lead II except that it was of slightly less voltage. Midaxillary T_3 did not look much like midaxillary T_2 or the limb T_2 or T_3, for the R-wave was short and was not notched. In the midaxillary Lead III there was a deep Q, however, as well as an elevation of the RS-T interval with a high take-off. The T also was inverted, but not as deeply as in the limb Lead III.

The blood pressure remained elevated. The patient died Oct. 5, 1935. The post-mortem examination showed a massive infarction of the posterior part of the left ventricle and interventricular septum in the region usually supplied by the right coronary artery. The infarction extended to within 1 cm. of the apex but did not

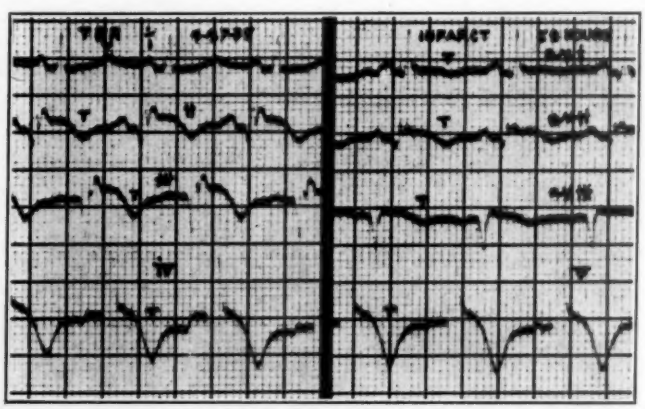

Fig. 13.—Case 19. Early T_3 type of electrocardiogram taken fifty-two hours after the onset of acute myocardial infarction. The inverted T_2 and T_3 elevated RS-T_2 and RS-T_3, deep Q_2 and Q_3 in the limb and midaxillary leads indicated T_3 type of infarct (posterior basal part of left ventricle) which was proved by post-mortem examination. The hypertension which persisted in spite of the acute infarction accounts for the inversion of the T in the midaxillary Lead I. The midaxillary T_1 is here shown to be more sensitive to left ventricular strain (hypertension) than the limb T_1, for the latter has remained upright.

reach to the apex. There was marked thinning of the posterior wall of the left ventricle about 2 cm. from the posterior part of the interventricular septum and about three-fifths of the distance from the coronary sulcus to the apex. A perforation had occurred at this point, and the pericardial cavity was filled with clotted blood. There were unusually large branches of the right coronary artery going to the infarcted region in the posterior part of the left ventricle and the posterior part of the interventricular septum. These vessels were markedly sclerotic and occluded by thrombi. They were of the size to be expected[9] when the right coronary artery is larger than usual and supplies more of the left ventricle toward the apex and toward the left than is found in the average heart. There was no infarction in the region supplied by the left coronary artery.

Case 19 shows the T_3 change in both the limb and midaxillary leads, but this change is shown better in the limb leads. The changes in the

midaxillary T_1 may best be interpreted as being a residual effect of the predominant left ventricular strain[1] from the hypertension, which showed better in the midaxillary Lead I than in the corresponding limb lead. (See comments and paper on ventricular strain[11] to follow.)

Table II shows a summary of these 2 cases and additional cases having evidence of only the T_3 type of infarct.

TABLE II

SUMMARY OF T_3 CASES. A COMPARISON OF T_2 AND T_3 CHANGES IN THE LIMB AND MIDAXILLARY LEADS

CASE	T_3 CHANGES MOST MARKED	T_3 CHANGES PERSISTED LONGER*, †
18	limb T_3‡	
19	limb T_2 & T_3	
20	limb T_3 sl., ‡	
21	limb T_3‡	
22	limb T_2 & T_3	
23	limb T_3 sl., ‡	
24	equal	
25	equal	mid-ax T_2
26	limb T_2 & T_3 sl.	
27	equal	mid-ax T_2 sl.,‡
28	mid-ax T_2 sl., ‡, ‖	
29	limb T_3§, ¶	
35	equal	
37	limb T_2 & T_3	

*Where nothing is recorded the patient was not followed long enough to determine changes.

†It was not possible in any case to show that the T_3 changes occurred earlier in the limb than the midaxillary leads, or vice versa.

‡Indicates changes in T_3 and T ax_3 are equal.

§Indicates T_3 and T ax_3 are equal.

‖T ax_1 is somewhat diphasic so there may have been some additional T_1 effect on T ax_2 besides the T_3 effect.

¶T ax_1 quite low but this patient had a previous hypertension so there may be some residual T_1 effect acting on T_2 also.

sl. Indicates slight difference.

In Table II there are listed 14 cases of the T_3 type of myocardial infarction. In 8 of these cases the T_3 change was shown better in the limb Lead II than in the midaxillary Lead II, in 1 case the change was greatest in the midaxillary Lead II, and in 5 cases the change was equal in the two sets of leads. The T_3 changes in the limb Lead III were greater than in the midaxillary Lead III in 5 cases, and equal to those in the limb leads in the remaining 9 cases. In no cases was it possible to determine whether the changes occurred earlier after infarction in the limb or in the midaxillary leads. In 2 cases the changes seemed to persist longer in the midaxillary Lead II than in the limb Lead II. In each case where the T_3 changes were present in the limb leads there was also definite change in the corresponding midaxillary leads. The midaxillary leads appeared to be of but little if any additional value in the T_3 type of infarction.

Six cases showed evidence of both the T_1 and T_3 abnormalities in their electrocardiograms. Two cases of this type in which post-mortem examinations were possible will be briefly described.

CASE 30.—Mr. C. R. H., aged forty-three years, was seen on March 9, 1935. He had had a few pains suggesting angina pectoris during the previous two years. During the week previous to the first electrocardiogram he had experienced six or seven attacks of substernal pain, either after meals or while at rest in bed, and one while climbing stairs. His last attack lasted at least fifteen minutes. Because of his frequent painful attacks even when at rest he was put to bed and kept quiet for about one month, and then was allowed to be up a little. On April 28, 1935, he was seized with a sudden severe abdominal pain. The urine contained blood. Morphine was required for relief. A diagnosis of left renal lithiasis was made. Two days later he had a marked pulmonary edema and then developed severe substernal pain considered to be acute myocardial infarction. A pericardial friction rub appeared.

The first electrocardiogram, which was taken on March 10, 1935, showed a depression of the RS-T interval in Lead I and elevation of this same interval in Lead III. In the corresponding axillary leads the same changes in the RS-T interval were present and were slightly more marked. There was a deep Q-wave in Lead III and in midaxillary Lead III. Leads IV and V were normal. The second

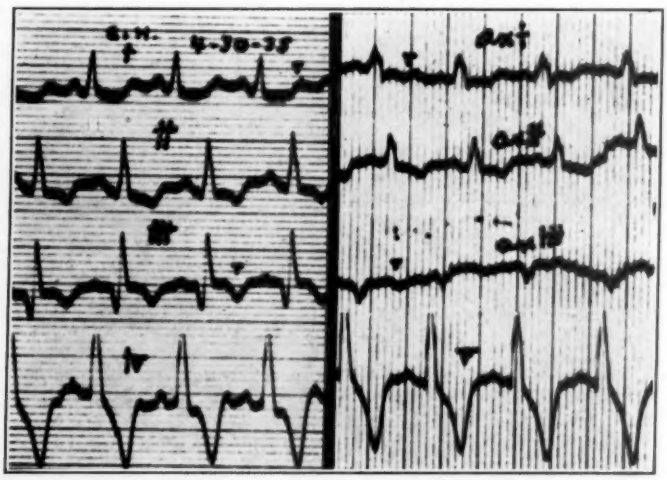

Fig. 14.—Case 30. Electrocardiogram two days after last acute myocardial infarction. The limb leads (i, ii, and iii) show a T_3 type of tracing with inverted T_2 and T_3 and deep Q_3. There is, however, a depressed RS-T_1 and RS-T_2 and a diphasic tendency to T_1 which suggest a possible T_1 change also. In the midaxillary leads (ax_I, ax_{II}, ax_{III}) the T_3 change is not well shown, while the T_1 is, the RS-T and T in midaxillary Leads I and II being quite similar. Autopsy showed both T_1 and T_3 types of infarcts.

tracing (Fig. 14) was taken about twelve hours after the development of the acute myocardial infarction, and a depression of the RS-T interval still remained in Lead I and in midaxillary Lead I, with the T-waves becoming diphasic. T_3 was inverted in the limb and midaxillary leads, but the inversion was more marked in the limb lead. T_2 was inverted but midaxillary T_2 was really diphasic. Q_4 and Q_5 were shortened and T_4 and T_5 more deeply inverted. Q_3 was deep. In the limb leads this was an electrocardiogram of the T_3 type and suggested infarction in the posterior part of the left ventricle in the part usually supplied by the right coronary artery. The midaxillary leads, however, were not so typical. Both the midaxillary T_1 and T_3 were diphasic. The T and RS-T in midaxillary Lead II resembled that of Lead I more than that in Lead III.

When there are changes in the T and RS-T in all three leads Barnes and I found such a comparison of Lead I or Lead III with Lead II was often a help in deter-

mining whether we were dealing with a T_1 type or T_3 type of tracing. This case, according to this observation then, would suggest a T_1 type of tracing in the midaxillary leads and a T_3 type in the limb leads.

The autopsy showed a stone lodged in the left ureter and a recent infarction of the midportion of the posterior part of the left ventricle. At the site of the infarct the heart was practically perforated, but pericardial adhesions had kept the heart from actually rupturing. There was also an acute infarction of the upper portion of the posterior part of the interventricular septum. These infarctions were all in the region supplied by the right coronary artery. There was no infarction in the right ventricle. There was an old fibrous endocardial and subendocardial infarction in the anterior portion of the interventricular septum where supplied by the left coronary artery.

The second electrocardiogram in the limb leads in Case 30 was of the T_3 type and showed a true picture of the recent infarct, which was in the usual site and was produced by a right coronary artery lesion. The depression of the RS-T interval in Lead I and in midaxillary

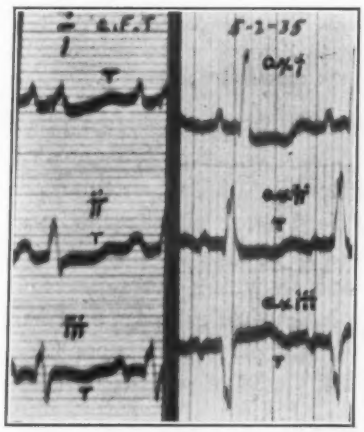

Fig. 15.—Case 31. Electrocardiagram taken just before death from pulmonary edema in a patient with multiple infarcts proved at autopsy to be of T_1 and T_3 types. In the limb leads (I, II, III) the T_2 is diphasic and T_3 inverted, suggesting a T_3 type of change but the RS-T_1 and RS-T_2 have a low take-off which has modified the changes in T_2. The T is diphasic in all of the midaxillary leads (ax_I, ax_{II}, ax_{III}) but is similar in midaxillary Leads I and II and midaxillary III is the reciprocal or invert of midaxillary Lead I. The RS-T depression in midaxillary II also is similar to the change in midaxillary I. The midaxillary tracing is of the T_1 type, while the limb leads show some T_3 changes.

Lead I was probably a result of the old anterior infarct, as these findings showed in the first tracing and were not entirely effaced by the later right coronary artery lesion. It is to be noted that the T_1 type of change was manifested better in the midaxillary leads and the T_3 changes were better displaced in the limb leads.

CASE 31.—Mr. C. F. T., aged sixty-eight years, was seen in consultation with Dr. George Carlisle, of Dallas. This patient had had a number of attacks of acute myocardial infarction. His blood Wassermann reaction was strongly positive but he had no sign of aortitis or aneurysm. He had had previous electrocardiograms which showed, on July 24, 1935, an inverted T_2 and T_3, on Feb. 7, 1934, a diphasic T_2 and an inverted T_3, on Dec. 7, 1934, a diphasic T_1 and inverted T_2 and T_3. Another

electrocardiogram (Fig. 15) taken when the patient was in extremis, just before death from pulmonary edema, showed, besides numerous premature ventricular contractions, a diphasic T_2 and an inverted T_3, suggesting a T_3 type of tracing. RS-T_2 was slightly depressed and there was a low take-off of RS-T_1. In the midaxillary leads all 3 T-waves were diphasic, but T_2 was similar to T_1 and not like T_3, suggesting a T_1 type. In the midaxillary leads RS-T_1 and RS-T_2 were depressed below, while the RS-T_3 was elevated above the isoelectric line.

The post-mortem examination showed that the heart weighed about 400 gm. There was a thinning out of the left ventricle wall from an old massive infarct involving the anterior part of the left ventricle and the apex with almost aneurysmal dilatation of the apex and with old adhesions of the apex to the pericardium. This region was supplied by the left coronary artery. Small depressions on the pericardial surface leading to the discovery of infarcts of the perpendicular or penetrating artery type, which I have previously described,[9] were found in the posterior basal part of the left ventricle where usually supplied by the circumflex branch of the left coronary artery and also where usually supplied by the right coronary artery. In this case, as occurs in about 10 per cent of hearts,[9] the entire posterior surface of the left ventricle was supplied by the left coronary artery. It has been shown[10] that the portion of the heart involved, and not the particular artery supplying it, determines the electrocardiographic findings in case there is a variation from the normal blood supply.

As far as the limb leads were concerned in Case 31 there was not much evidence of anything but the T_3 type of infarct, except in the electrocardiogram of Dec. 7, 1934, when the T_1 was diphasic and suggested the possibility that there also might be associated a left coronary artery lesion with a T_1 type of infarct. The final electrocardiogram, and the only one in which the midaxillary leads were taken, suggested in the limb leads that a T_3 type of infarct was present and in the midaxillary leads suggested a T_1 type. This seeming discrepancy really was an indication that the patient had both susceptible regions of the heart involved and this and other cases of this series suggest that the limb leads are more sensitive to the T_3 type of infarcts and the midaxillary leads more sensitive to the T_1 type.

TABLE III

SUMMARY OF CASES SHOWING BOTH T_1 AND T_3 CHANGES. A COMPARISON OF THE T_1 AND T_3 CHANGES IN THE LIMB AND MIDAXILLARY LEADS IS SHOWN

CASE	DATE OF ELECTROCARDIOGRAM	LEADS IN WHICH T_3 CHANGES WERE BEST SHOWN	LEADS IN WHICH T_1 CHANGES WERE BEST SHOWN	INDICATIONS OF BOTH T_1 AND T_3 CHANGES WERE SEEN
30	3/10/1935	equal	equal	limb & ax
	4/30/1935	limb	ax	limb & ax (?)
31	5/ 2/1935	limb	ax	limb
32	4/21/1936	limb	ax	ax
	4/22/1936	limb	ax	ax
33	7/ 6/1931	limb	*	*
	11/ 2/1934	limb	ax	limb
34	8/ 4/1936	equal†	equal	limb & ax
36	11/16/1936	limb	ax	ax

*Midaxillary leads were not taken in this electrocardiogram.

†This case had a previous electrocardiogram of the T_3 type only, in which only the limb leads were taken.

The 2 cases described and 4 additional cases having electrocardiograms suggestive of both the T_1 and T_3 type of infarct are shown in Table III. Although this series is small, 2 cases were verified by autopsy. A glance at the table indicates what has already been suggested, namely, that in most cases and in most of the electrocardiograms taken on cases of this type the T_3 infarct is better shown in the limb leads, while at the same time the T_1 type is better revealed in the midaxillary leads. In most instances the limb leads, while registering the posterior or T_3 type of infarct, also gave some suggestion or indication of a possible T_1 type of lesion. In two electrocardiograms the multiple infarcts seemed to be shown equally well in the limb and midaxillary leads. The T_1 change noted in the limb leads in combined T_1 and T_3 types of infarcts was a slight RS-T_1 depression with or without a diphasic element in the T-wave in Lead I. That these limb lead T_1 changes were not always present in combined T_1 and T_3 types of infarcts is seen in Case 32 in which the first electrocardiogram failed to show evidence of the T_1 type of infarct in the limb Lead I although it was clearly seen in the midaxillary Lead I.

It is interesting to note that in the normal electrocardiogram the midaxillary T_3 is more frequently inverted than the conventional T_3. In the presence of lesions tending to produce the T_1 change or in multiple infarctions of T_1 and T_3 type the midaxillary T_3 eventually is more likely to become positive than is the conventional T_3. Thus, all three midaxillary leads appear to be more sensitive to T_1 changes than the limb leads, even in the presence of a T_3 type of lesion.

COMMENT

Space has not permitted a detailed description of all of the cases of myocardial infarction which have been studied with the midaxillary leads. It is to be regretted that the series is so small and the post-mortem examinations are so few. There have not been many deaths among the group of patients studied and, unfortunately, the post-mortem examinations which were made were performed on patients whose electrocardiograms had indicated T_3 or combined T_1 and T_3 types of infarcts. Regardless of the paucity of post-mortem proof there is enough evidence based on our previous knowledge of the electrocardiographic localization of myocardial infarcts in the limb leads, which also were studied in each case, to indicate that the midaxillary leads accurately indicate the site of the infarction.

In all of the cases reported in this paper the right and left arm electrodes were placed in the corresponding midaxillary lines. Since infarction produced by a lesion of the left coronary artery is generally in the anterior part of the heart it was thought that this lesion might be shown better if the axillary electrodes were placed in the anterior axillary lines, rather than in the midaxillary position. Such a lead

does show greater amplitude of the T and the various other waves in Lead I and greater inversion of the T in the presence of a T_1 type of infarction, but as yet no evidence has been obtained to indicate that this lead is any more accurate or reliable than the midaxillary Lead I. Conversely, it might be expected that electrodes placed at the right and left posterior axillary line might show the T_3 changes of posterior infarcts best but this does not seem to be true in the few cases studied with these leads.

In a few cases Leads I, II and III were taken in all possible combinations, with the right arm electrode placed first on the right arm, then the right anterior, middle, and posterior axillary lines, and the left arm electrode attached to the left arm, left anterior, middle, and posterior axillary lines. None of these possible positions for the electrodes seemed to be superior to the midaxillary leads. The important point that was noted was that, as far as the T-wave inversion in Lead I was concerned, this inversion became progressively deeper in the following order as the leads approached the level of the heart: right arm to left arm, right midaxillary line to left arm, right arm to left midaxillary line, and right midaxillary line to left midaxillary line. No effort was made to determine differences in the electrocardiogram in the upper and lower levels in the midaxillary lines, for small electrodes were not used, the tests being confined to the use of the larger linear electrodes commonly used, at least until recently, in clinical electrocardiography.

Since the midaxillary leads pass through the heart from side to side they do not resemble Leads IV and V of Wolferth and Wood,[13] which pass through the heart in an anteroposterior direction. The midaxillary leads resemble more closely the standard limb leads. Since the thorax is narrower anteroposteriorly than laterally and the heart occupies more of the anteroposterior diameter than the lateral, one would expect to find Lead IV to be more sensitive than the midaxillary leads, and in the main this appears to be true. This would seem to place the midaxillary leads intermediate between the limb and anteroposterior leads as far as their sensitivity for T_1 changes is concerned. In general, then, we find that the limb Lead I is not as sensitive as might be desired for T_1 changes and is likely to be unchanged unless considerable pathologic damage has resulted. It is the author's impression that the anteroposterior leads go to the other extreme and may at times be a little too sensitive and show abnormality when clinically one is unable to account for it. In the absence of changes in the limb or midaxillary leads one must be a little cautious in interpreting diphasic and occasionally upright T, slight changes in the level of the RS-T segment or slight shortening or lengthening of the Q in the anteroposterior leads as always indicating cardiac abnormality. Marked changes in the anteroposterior leads appear to be more reliable. The

midaxillary leads appear to be enough more sensitive than the limb leads to show T_1 changes better, but not enough so to show changes that cannot be accounted for on a pathologic basis. Even though the anteroposterior leads seem to be more easily altered from the normal than the limb or midaxillary leads, some cases were studied in which, in the presence of T_1 changes in the limb leads, the anteroposterior leads remained normal (as in Case 2, Figs. 6 to 10). This indicates that in the future electrocardiography cannot be confined to a study of three or four leads without interfering with progress. Just what leads will eventually be found the most satisfactory is not known at present. More experimentation is needed. Other leads, such as Weinstein's[8] "multiple plane" leads, must be evaluated.

Leads IV and V have complicated electrocardiography, not so much because of the additional leads required, as from the necessity of developing a new standard for normal and abnormal in leads where all complexes, in fact, the whole tracing is inverted. This difficulty is not encountered in the midaxillary leads, for the right arm electrode is not placed closer to the heart than the left, so all of the complexes are normally upright.

The addition of three more leads would make electrocardiography more tedious. Since the midaxillary leads show the T_1 changes and not the T_3 changes more advantageously than the limb leads there is no real necessity for taking the midaxillary Lead III. Furthermore, any T_1 change likely to alter midaxillary Lead II is almost certain to change midaxillary Lead I to a more marked degree, so midaxillary Lead II also can be omitted. Thus, with the addition of only one more lead,* the midaxillary Lead I, or as it might be called, the lateral thoracic lead, it is possible to depict practically any significant T_1 change that these three midaxillary leads might show. If the midaxillary Lead I shows significant abnormality, then, if one desires, the midaxillary Leads II and III also may be taken, but very little additional information is likely to be gained except possibly in combined T_1 and T_3 changes.

In several cases there was a seeming contradiction, in that the limb leads suggested the T_3 type of infarction and the midaxillary leads the T_1 type (Table III). That both systems of leads were correct was seen in two of the cases that came to post-mortem examination, as infarction in the location anticipated for both the T_1 and T_3 electrocardiographic changes was found in each of these cases. In the remaining cases of this group there was a history of multiple acute coronary episodes. Furthermore, in 4 of the 6 cases in Table III there were some changes in the RS-T level and T in Lead I of the limb leads that suggested that there might also be an associated T_1 type

*It must be understood that the midaxillary Lead I is not recommended for, or even suggested as a substitute for, or to replace, the conventional limb Lead I.

of lesion. Electrocardiograms of the limb leads, such as those of Fig. 14 and Fig. 15, are of this character. Cases in which, in the presence of inversion of T_2 and T_3, there is also a diphasic or inverted T_1 should make one suspect a possible T_1 type of lesion, in addition to the T_3. Barnes and I found a number of these cases with changes in all three leads and suggested that eventually, if successive or serial electrocardiograms were taken, they generally would reveal the more recent or more predominant infarction or ventricular strain, in the absence of digitalis effect or pericardial adhesions. The rule, which has been previously referred to, and which Barnes and I followed in the interpretation of the T type of change in the electrocardiogram in some of these more difficult cases where there is some change in all three limb leads, was to observe carefully the T and RS-T in Lead II and determine whether it more nearly resembled the corresponding segments of Lead I or of Lead III. If it resembled Lead I we considered the tracing to be of the T_1 type, and if it resembled Lead III, we considered it to be of the T_3 type. This general rule has been followed in the interpretation of the electrocardiograms in the cases listed in Table III, and observation of this rule enables one to obtain a little additional knowledge from an electrocardiogram, even if confined to the limb leads. In these cases of combined T_1 and T_3 lesions, however, it was observed that the T_1 type showed best in the midaxillary leads, even in the presence of a rather extensive lesion generally associated with the T_3 type of electrocardiogram. Since the limb leads show the T_3 change the best and the midaxillary show the T_1 best it should be a little easier to recognize these multiple infarctions with both the T_1 and T_3 types of lesions without the necessity of repeated tracings.

When Barnes and I[2] stated that the electrocardiogram had a tendency to reveal the more recent, or more predominant, lesion it was not known at that time that the limb lead electrocardiogram registered T_3 changes in infarction more readily than T_1 changes, and one must take this factor into consideration. With the addition of the midaxillary leads to bring out better the electrocardiographic changes of a T_1 lesion, even in the presence of an associated T_3 type of lesion, our statement may more frequently be found to be correct, as it now may become a little easier to determine the more recent, or more predominant, lesion as well as to recognize an old T_1 type of lesion in the presence of a recent T_3 type, or vice versa.

It should not be assumed that the midaxillary leads are altered only by infarction. Like the limb leads they are altered also by digitalis, pericarditis, and strain working predominantly on one ventricle. Discussion of the effects on the midaxillary leads of conditions other than infarction is reserved for a publication[11] that is to follow. In diseases of the heart other than infarction the midaxillary leads, and

especially midaxillary Lead I, appear to act similarly to the limb leads, except that here again the midaxillary leads register changes in the T-wave in Lead I (chiefly inversion of the T) to a more marked degree, and the changes in the midaxillary leads appear to begin earlier and to last longer. This is especially true of the T_1 or T_1 and T_2 inversion of predominant left ventricular strain which may be observed in hypertension, aortic stenosis, and aortic regurgitation. As might be anticipated, the midaxillary leads are apparently not quite as sensitive as the limb leads to the T_2 and T_3 inversion in predominant right ventricular strain.

There are some who object to the introduction of additional electrocardiographic leads. No one can ignore the valuable contributions made to our knowledge of the heart and its action in health and disease, which have resulted from a study of the three standard limb leads. It is hoped that they may continue to add to our knowledge. But, after the monumental work of Wolferth and Wood, we cannot overlook the possibility that, for some purposes, additional leads may augment our knowledge and that leads may be found which may depict more easily or more accurately certain types of cardiac lesions. This paper has suggested that the midaxillary Lead I may be of some additional help in the T_1 type of infarction, which does not register as well as we would like in the limb leads. The paper to follow[11] suggests that the midaxillary Lead I is more sensitive and more easily changed in predominant left ventricular strain than is the corresponding limb lead. It is hoped that others may become interested in research on this subject and that with greater facilities at their command may be able to determine the true worth of the leads here suggested. Perhaps, in addition, leads which are still more sensitive than the ones described here, but which will accurately show T_1 changes, will be found.

CONCLUSIONS

1. The electrocardiogram can be made somewhat more sensitive to the T_1 type of changes associated with infarction in the part of the heart usually supplied by the left coronary artery if Lead I is taken so that the current passes more directly through the heart rather than entirely above it, as in the standard Lead I. Clinical trial of numerous lateral thoracic and arm-to-thorax leads showed the midaxillary leads to be the most satisfactory for this purpose.

2. The normal waves in the midaxillary leads are similar to those of the limb leads and all deviations from the normal appear to have the same significance as in the standard leads.

3. Normal control patients were not found to show any abnormalities of the T-wave or RS-T segment or Q except in midaxillary Lead III.

4. In myocardial infarction, as a rule, the midaxillary leads are found to show T_1 changes more readily than the corresponding limb leads.

These changes in some cases were seen to come earlier, in most cases to show more markedly, and in some cases to last longer in the midaxillary leads than in the limb leads. The T_3 type of infarction was recorded better in the limb leads for the most part, although in some cases this was not true.

5. In no case did inversion of T_1 or T_2 or significant depression or elevation of the RS-T_1 or RS-T_2 occur in the midaxillary leads unless there was definite reason to suspect cardiac damage. In no instance was inversion of the T_1 in the limb leads not associated with equal or greater inversion of the T_1 in the midaxillary leads.

6. The amplitude of the waves in the midaxillary Lead I generally is greater than in the standard Lead I. This alone does not account for the midaxillary Lead I appearing to be more sensitive to T_1 changes, as, for example, T-wave inversion was found in this latter lead when in the standard limb lead the T was merely diphasic or isoelectric, or even upright (positive).

7. In combined infarctions of the T_1 and T_3 types, the T_3 type is, as a rule, recorded best in the limb leads, while the T_1 generally is best shown in the midaxillary leads. It is possible, then, to find electrocardiographic evidence of both infarctions at one time.

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USE OF THE BARIUM-FILLED ESOPHAGUS IN THE X-RAY STUDY OF ABNORMALITIES OF THE HEART AND THE AORTA*

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THE use of the barium-filled esophagus in the roentgen diagnosis of the heart and aorta has attained sufficient vogue to make it advisable at the present time to consider its value and its limitations. Following the demonstration of the relationship of the esophagus to

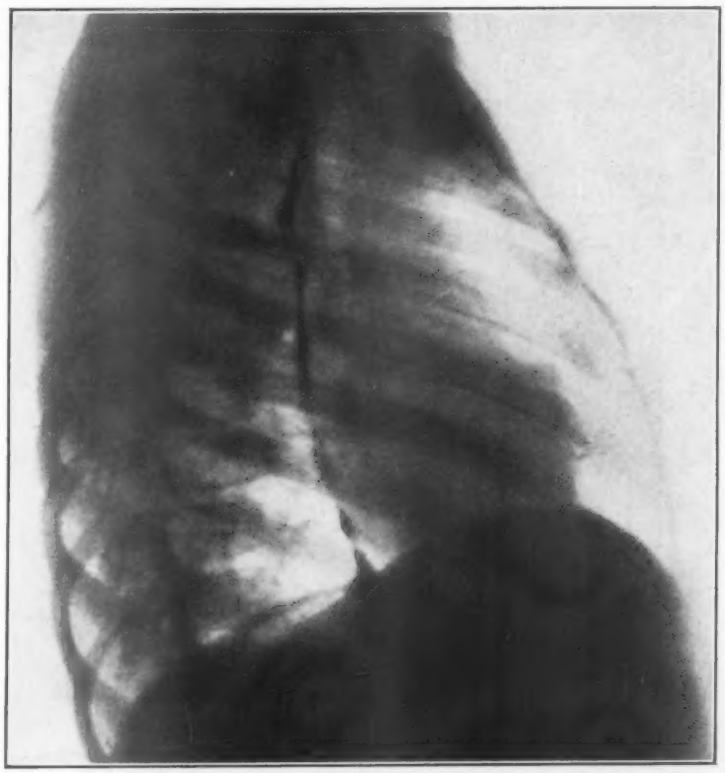

Fig. 1.—Normal heart in the right oblique position. The vertical course of the esophagus is indented by the aortic arch.

enlargement of the left auricle,[1] the barium-filled esophagus assumed a prominent rôle in the diagnosis of enlargement of that chamber. In the routine cardiac examination of all medical cases at the Montefiore Hospital extensive use is made of this important diagnostic aid. In the past four years there have been a number of instances in which the

*From the Radiographic Service of Dr. A. J. Bendick, and the Medical Service of Dr. L. Lichtwitz, Montefiore Hospital.

accepted criteria of posterior displacement of the esophagus in the right oblique view for the diagnosis of an enlarged left auricle have failed of confirmation. At post-mortem examination no enlargement of this chamber could be demonstrated.

This necessitated reexamination of the criteria for left auricular enlargement, and investigation into other causes for similar displacement of the esophagus. A case observation[3] (M.C.), published by myself and Dr. E. B. Gutman, offered a clue, subsequently corroborated by a large number of cases, that elongation of the aortic arch was responsible for most of the confusion.

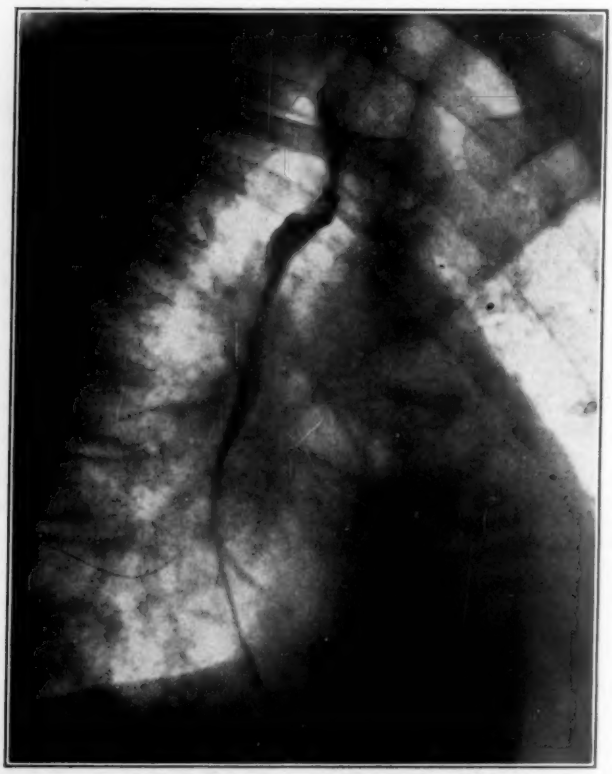

Fig. 2.—Left auricular enlargement displacing esophagus posteriorly. Same patient as in Fig. 3.

In order to clarify the subject a brief review of the anatomical relationship is of sufficient importance to be presented here. The esophagus pursues a downward course anterior to the bodies of the thoracic vertebrae slightly to the left of the midline up to a point a few inches above the diaphragm where it deviates to the left to enter the abdomen. In its course it is compressed on its left side by the arch of the aorta to which it is attached by areolar and loose fibrous connective tissue. Below the area of compression the esophagus lies behind the posterior surface of the left auricle and anterior to the aorta. In the normal

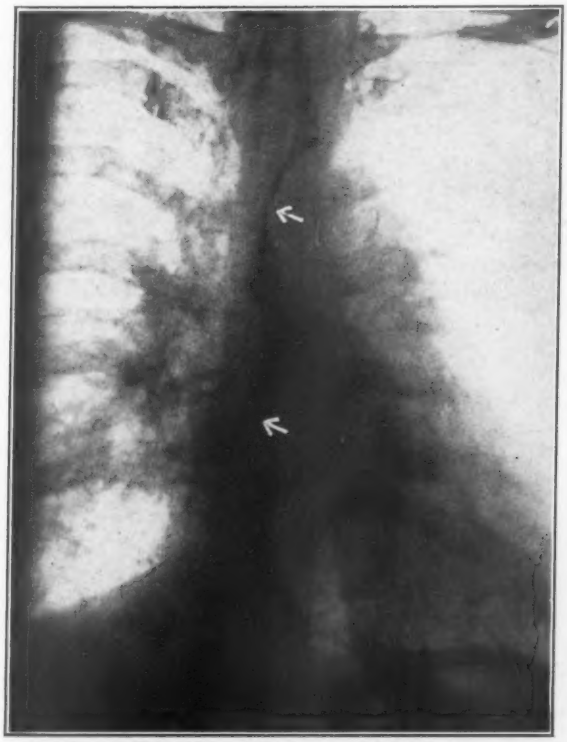

Fig. 3.—Note the left auricular impression on the esophagus. It is compressed and displaced to the right.

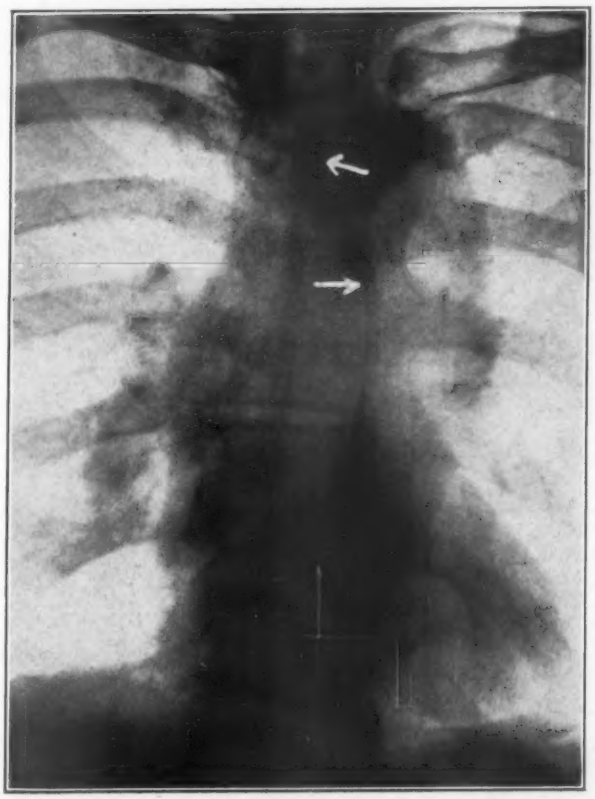

Fig. 4.—The upper arrow shows compression to the right by the aortic arch. The lower arrow indicates deviation to the left in the postero-anterior position.

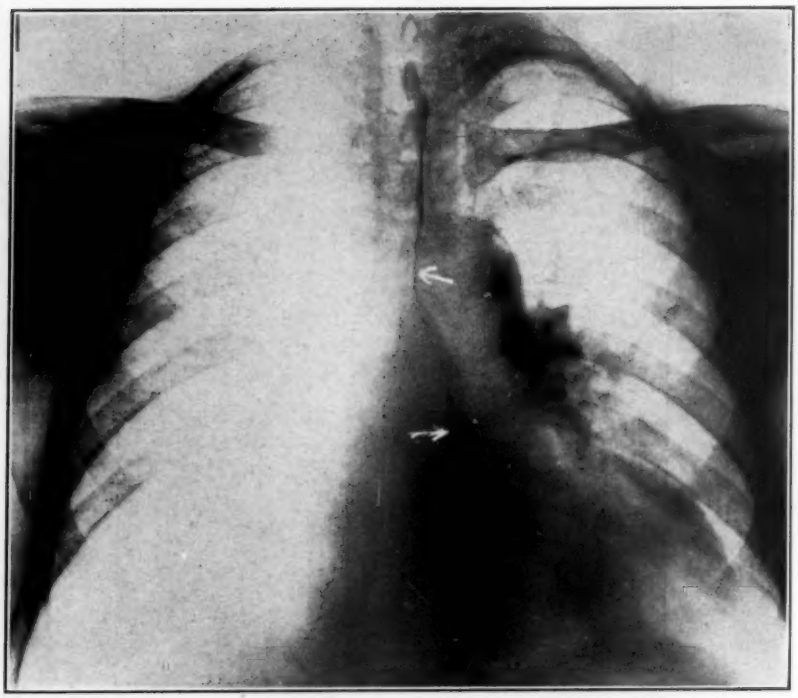

Fig. 5.—Barium displacements similar to those in Fig. 4.

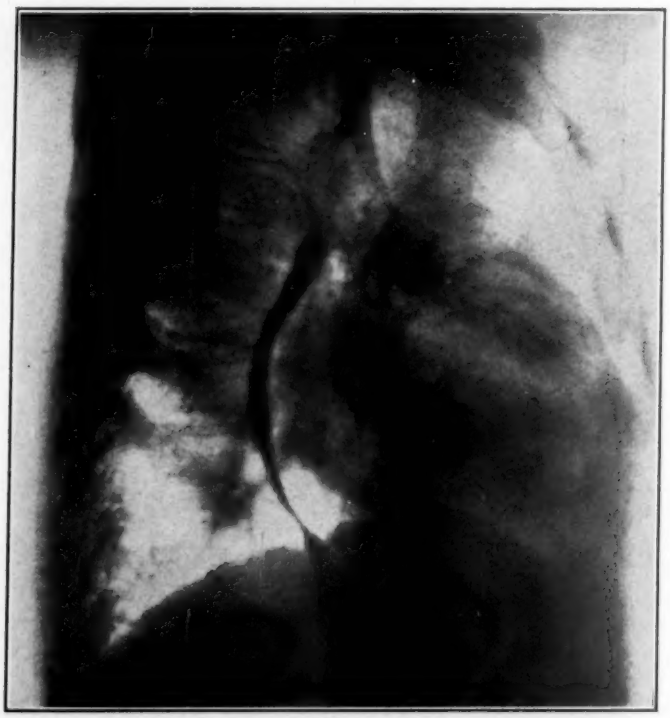

Fig. 6.—Though the left auricle definitely occupies the mid third of the retrocardiac space denoting left auricular enlargement (proved at autopsy), a space is observed between the left auricle and the esophagus. The length of the aortic arch pulled the esophagus sufficiently posteriorly that it no longer was in close relationship to the posterior surface of the heart. Same patient as in Fig. 5.

subject this space between the aorta and the left auricle measures but a few centimeters and this is occupied by the esophagus.

In conditions affecting the length of the aorta, such as is commonly seen in hypertension, arteriosclerosis, and aortic insufficiency, the esophagus, because of its attachment to the aorta, may be pulled posteriorly, increasing its distance from the posterior surface of the heart (left auricle). In aortic elongation, especially of the transverse portion of the arch, the esophagus is pulled not only posteriorly but also to the left, so that it no longer lies anterior to the vertebral bodies but rather in the left costovertebral gutter. This traction to the *left* and *posteriorly* is a key to the use of the barium-filled esophagus in the differential diagnosis of enlargement of the left auricle and the elongation of the aortic arch.

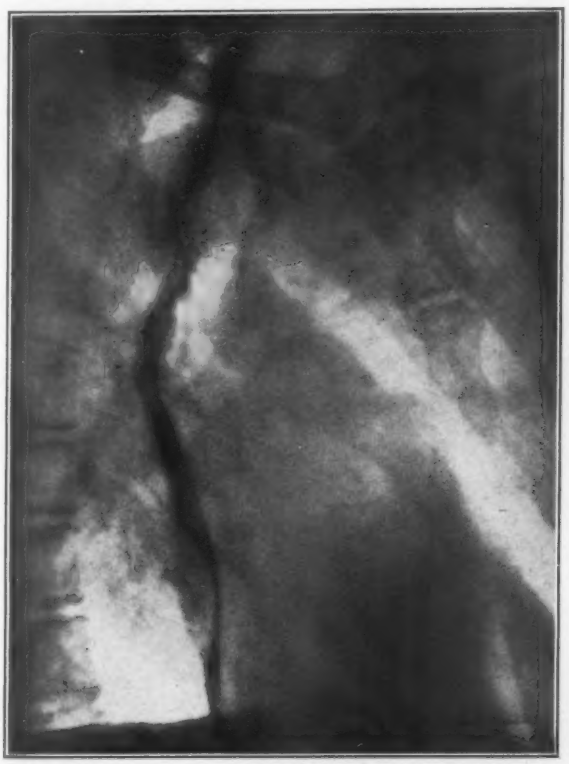

Fig. 7.—Same patient as in Figs. 4 and 9. The marked tortuosity of the elongated aorta is reflected by the appearance of the esophagus within the heart shadow.

Here it may be emphasized that displacement posteriorly and to the left does not occur in all cases of elongation of the aorta. It occurs only in those cases where elongation of the arch of the aorta is associated with adhesions, sufficient to displace the esophagus. These adhesions occur in over three-fourths of the adult post-mortem material, and they occur at and just below the area of aortic compression of the esophagus.

The examination of the heart consists of the fluoroscopic observation of the course of a swallowed spoonful of barium paste in the postero-anterior, right oblique, and left oblique positions. Radiographic films are useful for permanent record only.

In the normal heart the course of the esophagus is vertical (Fig. 1). The normal indentation of the aorta is seen in the postero-anterior and right oblique positions. In the left oblique view the indentation is generally less prominent. Below this indentation the course is vertical in all radiographic positions.

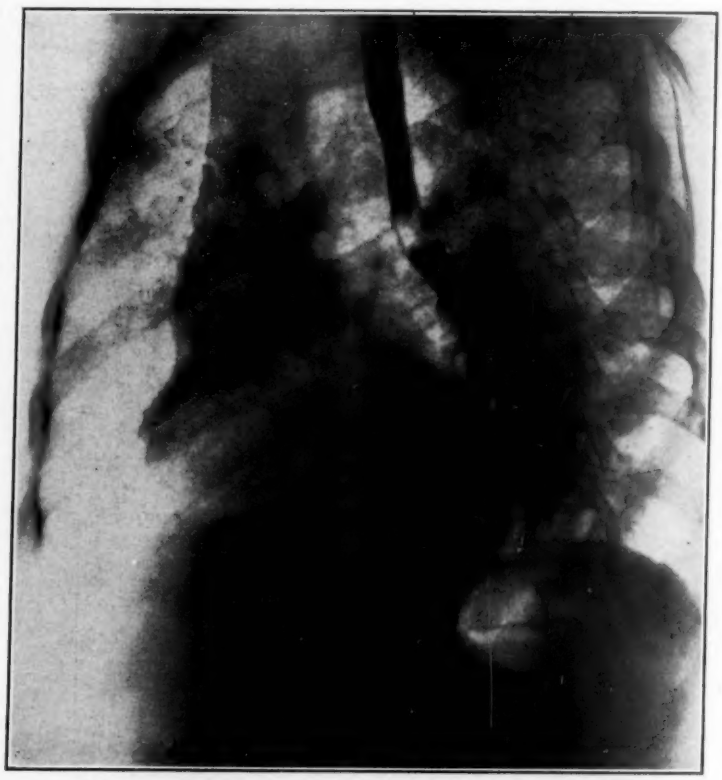

Fig. 8.—Same patient as in Figs. 5 and 6. Note posterior deviation of the esophagus due to adhesions just below the aortic compression. Left oblique position.

Enlargement of the left auricle displaces the esophagus posteriorly, as seen in all degrees of rotation into the right oblique position. In the postero-anterior position the barium-filled esophagus (Fig. 2) is either compressed or displaced to the *right* by the enlarged left auricle (Fig. 3). The course of the esophagus below the aortic indentation remains vertical.*

*Rarely is there displacement of the barium-filled esophagus to the left in the postero-anterior position. In such cases in the left oblique position, however, the posterior displacement does not take place at the aortic indentation of the barium-filled esophagus. This rare group will be taken up in greater detail in a subsequent report and apparently involves mass relationships between the right ventricle and both auricles.

With elongation of the transverse portion of the aortic arch associated with adhesions, a barium-filled esophagus will be pulled to the left in the postero-anterior view. This traction takes place just below the area of compression of the aortic arch. Thus, while the area of aortic compression of the esophagus is to the right the traction below pulls the esophagus to the left (Figs. 4, 5). The esophageal displacement of an enlarged left auricle usually is at a somewhat lower level.

In the left oblique view the esophagus is pulled posteriorly below the clearly visualized aortic arch before resuming its vertical course (Figs.

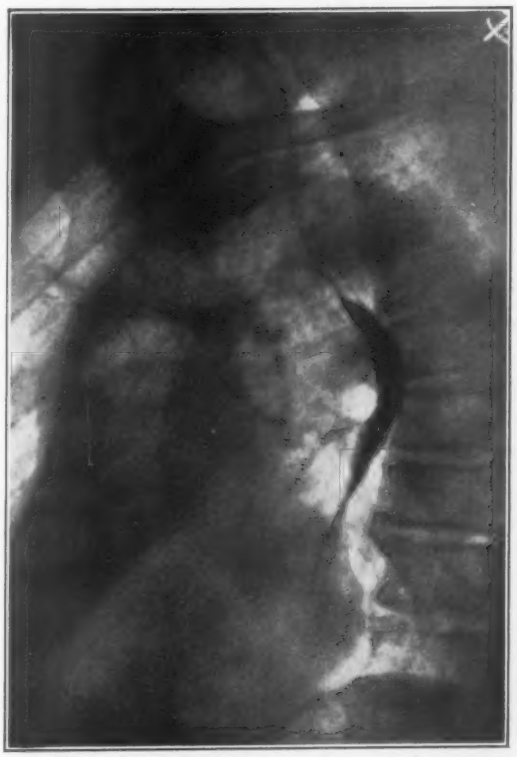

Fig. 9.—Same patient as in Figs. 4 and 7. Posterior pulling of the esophagus.

8, 9). In the right oblique position the esophagus may be pulled posteriorly, simulating left auricular enlargement. Careful rotation in several degrees of right obliquity will disclose the cause of the esophageal deviation, especially when in the postero-anterior view the deviation of the esophagus is to the *left*. The barium-filled esophagus may be drawn so far posteriorly as to leave a clear space between the esophagus and the left auricle (Fig. 6). In the right oblique view the esophagus may sometimes be seen within the heart shadow and on occasion it may seem even to be drawn anteriorly (Fig. 7), depending upon the degree of fluoroscopic rotation of the patient's heart and the degree of tortuosity

of the aorta. In this group, the deviation of the esophagus, it must be emphasized that the esophagus lies no longer in close relationship to the left auricle, but is drawn in even closer relationship to the descending thoracic aorta.

The posterior displacement of the esophagus where there is deviation to the left in the postero-anterior position cannot be maintained as a criterion of an enlarged left auricle. Enlargement of the left auricle in such instances must be judged by additional criteria such as a bulge into the middle third of the retrocardiac space as seen in the right oblique position, the appearance of the left auricle on the right border of the heart in the postero-anterior position, and the upward displacement of the left main bronchus as seen in the left oblique position.

Differentiation, by means of the barium-filled esophagus, between the groups of elongation of the aorta and of enlargement of the left auricle is of importance, especially in the fluoroscopic diagnosis of individuals in the forties and over. At Montefiore Hospital where a large proportion of the patients are of this age group I would estimate that fully one-fourth have esophageal displacement to the left in the postero-anterior position. This group undoubtedly formed a large proportion of our errors in the estimation of the degree of enlargement of the left auricle. Since this differential method has come into use the percentage of error must be considerably less.

SUMMARY

1. Posterior displacement of the barium-filled esophagus, as seen in the right oblique position, and its displacement to the right in the postero-anterior position are due to left auricular enlargement.

2. Deviation of the esophagus to the left below the area of aortic indentation in the postero-anterior position, and posteriorly in the left oblique position, is due to elongation of the transverse portion of the aortic arch.

3. The use of the barium-filled esophagus serves to differentiate elongation of the transverse portion of the aortic arch from left auricular enlargement.

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A MOBILE UNIT FOR SIMULTANEOUSLY RECORDING HEART SOUNDS, PULSE TRACING, AND ELECTROCARDIOGRAM*

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FOR the past five years we have been recording heart sounds and pulse tracing simultaneously, using several different methods and numerous experimental assemblies. For heart sounds we have used the Einthoven method with a string galvanometer, the Wiggers-Dean

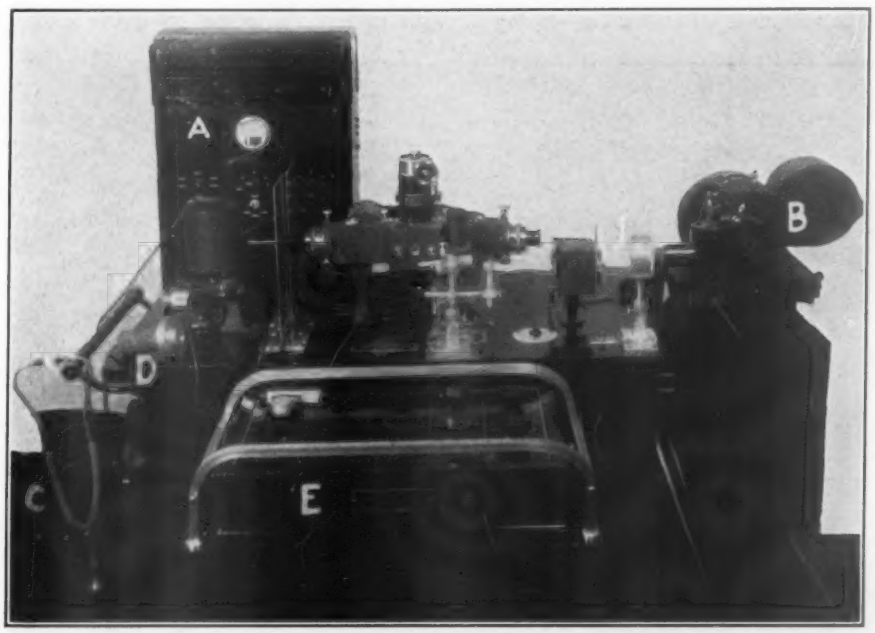

Fig. 1.—The complete unit. *A*, Amplifier; *B*, camera; *C*, earphone with stethoscope attachment; *D*, crystal microphone; *E*, electrocardiograph control box.

capsule method with modifications, and finally a method employing a microphone, vacuum tube amplifier, and recording galvanometer. The apparatus and technic have been sufficiently standardized now to allow tracings to be made routinely. We are reporting the present assembly which has the advantages of simplicity and compactness.

The unit herein described was built around a Cambridge mobile electrocardiograph No. 3 (Figs. 1 and 2). The apparatus has several advantages: (1) The entire unit is self-contained and mobile; (2) the cost

*From the Cardiovascular Laboratory, Department of Physiology, and the Heart Station, Michael Reese Hospital, Chicago.

of the heart sound and pulse tracing equipment is relatively low; (3) the unit is easy to use and has few adjustments; and (4) it is accurate and gives consistent results.

HEART SOUND EQUIPMENT

The apparatus for recording the heart sounds consists of a microphone, a three-stage amplifier, and a small galvanometer. The amplifier was designed and built by one of us (H. M.), and, with the microphone and galvanometer, it was used clinically by Sacks, Marquis, and Blumenthal[1] and Sacks and Marquis.[2]

The microphone is of the piezo electric crystal type, which was found to be most suitable because it is "light, portable, inexpensive, does not require the use of any special transformer or batteries, and will operate in any position without any background noise or hiss."[2]

The amplifier is battery operated, and consists of two type 32 tubes in the first two stages and a type 33 in the power stage, all resistance-capacity coupled (Fig. 3). The volume is controlled by varying the grid bias of the second tube, and a frequency-control potentiometer is connected across the output of the power stage. Two output jacks are provided, one for connecting the galvanometer, and the other for connecting simultaneously a single earphone receiver with a stethoscope attached so that the operator may hear the sounds that are being recorded (Fig. 4). Before the last stage there is a band pass filter circuit which passes only the narrow band between 50 and 70 cycles. This is for the purpose of picking up the low-pitched murmurs which may ordinarily escape notice. This filter may be cut in or out of the circuit by means of a switch. Without the filter, the frequency range of response is approximately from 60 to 3,000 cycles.* It is extremely important that the parts be exactly as specified, and so arranged as to avoid any stray coupling. Proper shielding is also essential.

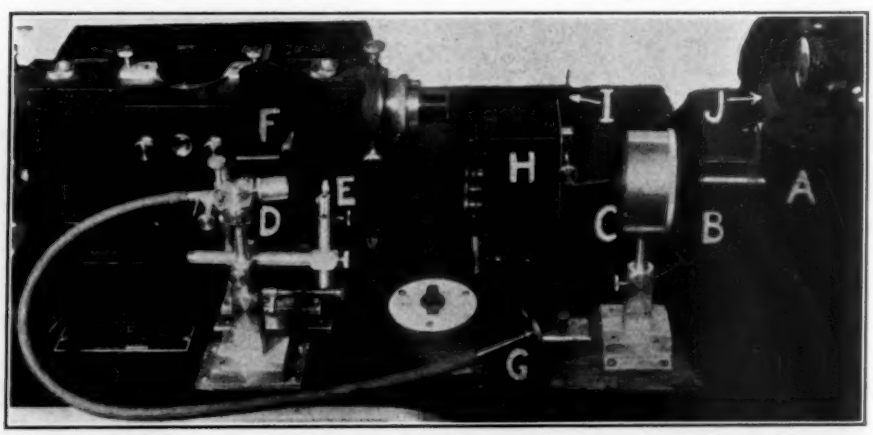

Fig. 2.—Close-up showing the heart sound and pulse tracing registration apparatus. *A*, Lamp housing; *B*, lens tube; *C*, housing for prism combination; *D*, segment capsule for pulse; *E*, small lens; *F*, heart sound galvanometer; *G*, pulse cup; *H*, timer; *I*, shutter; *J*, camera slot.

The galvanometer was obtained from the General Electric X-Ray Corporation; it is identical with the one used in their Victor Electrocardiograph. It consists of a permanent magnet, in the field of which a small iron plate carrying a small mirror

*These figures apply to the amplifier only. The galvanometer itself has a natural frequency of 200 c.p.s., which, when the higher frequencies are recorded, causes some distortion. This is not significant for practical purposes.

is suspended by a metal ribbon. Two circular coils are so placed within the magnetic field that the audio frequency currents flowing through them from the amplifier change the magnetic field and cause the iron plate and mirror to oscillate. The movements of a beam of light reflected by this mirror are recorded photographically. The mirror and plate are immersed in oil for damping.

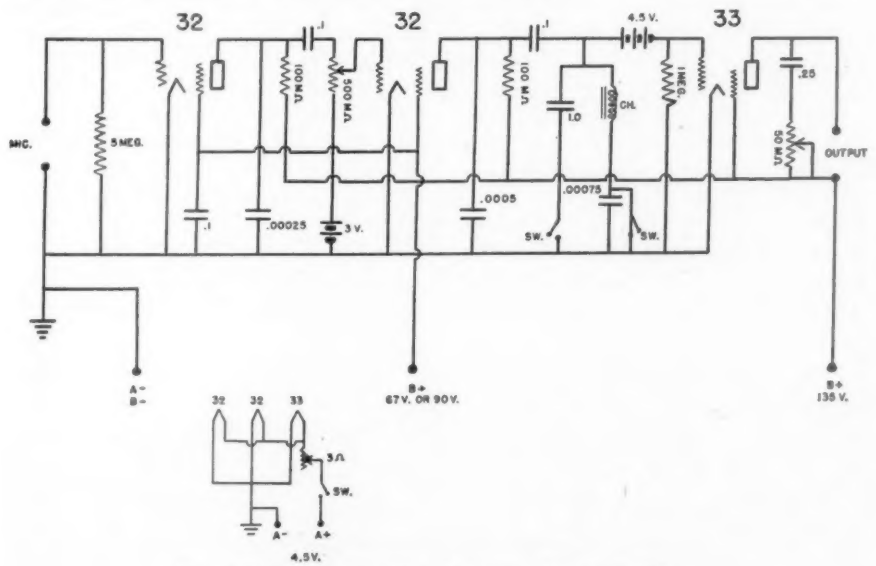

Fig. 3.—Schematic wiring diagram of the amplifier.

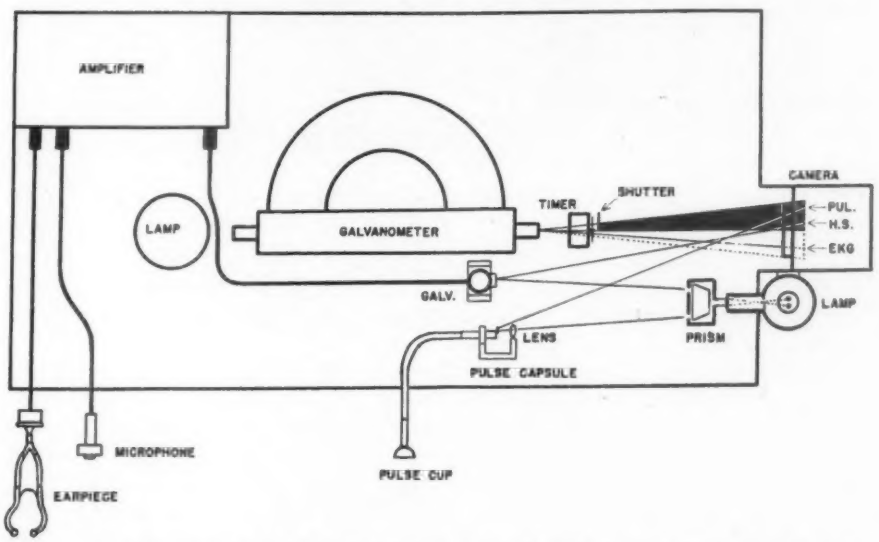

Fig. 4.—Diagram of top of electrocardiograph table showing arrangement of parts and paths taken by light beams.

For audible amplification of the heart sounds we are using a separate auxiliary unit consisting of a power amplifier and loud speaker designed for operation from the 110 volt D.C. line. The amplifier consists of a type 76 tube driving two 48's in push-pull.

PULSE TRACING EQUIPMENT AND LIGHT SOURCE

Optical registration of the pulse is accomplished by means of the usual Frank segment capsule method. The diagram in Fig. 4 represents a top view of the mobile electrocardiograph table and shows the arrangement of the pulse-tracing and heart-sound apparatus mounted on it. Figure 2 is a photograph of the actual equipment. The light source for both the heart-sound galvanometer and the pulse capsule consists of a Mazda automobile headlight bulb No. 1130, 32 c.p. It consumes 4 amperes at 8 volts, and it is operated directly from the 110 volt D.C. line with a 25 ohm, 4.5 ampere capacity resistance in series. The lamp is enclosed in a small, cylindrical housing having a short lens tube projecting from the front. Sliding over the lens tube is a second tube carrying a lens having a focal length of 2 inches and a diameter of 1 inch. Within the lens tube at the point where it joins the lamp housing, there is mounted a single, fixed, vertical slit approximately 1 mm. wide. The light bulb is turned with its socket so that the two parallel spiral filaments are in a line at right angles to the optical axis. This causes two narrow beams of light, almost parallel, to emerge from the center of the lens about 2 mm. apart. The unit immediately

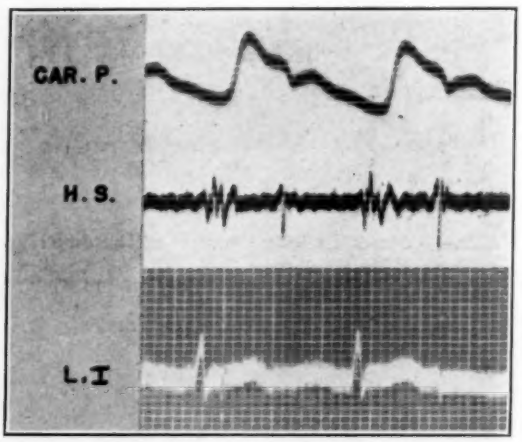

Fig. 5.—Simultaneous carotid pulse, *Car. P.*, heart sounds, *H. S.*, and electrocardiogram, *L. I.*

in front of the lens consists of a doubly reflecting combination of prisms taken from a colorimeter. The two beams of light enter the center of the prism combination and emerge from the front, one on each side, about 2 inches apart and parallel with the original paths.

One beam falls on the galvanometer mirror and is reflected onto the camera slit. The lens on the lamp housing is moved back and forth until this reflected beam produces, at the camera, a sharp image of the vertical slit. The small galvanometer (as well as the pulse tracing capsule) has two screws for adjusting the vertical and horizontal position of the beam.

The other beam falls on the mirror of the segment capsule, but in order that this reflected beam may be sharply focused on the camera without disturbing the focus of the first beam, it is necessary to introduce another lens in the path of the beam before it strikes the mirror on the capsule. This lens is ⅜ inch in diameter and has a focal length of 7 inches. By means of two small rods and clamps it is fastened to the stand which supports the capsule; its distance from the capsule is adjusted until the reflected beam is also sharply focused on the camera (approximately ¾ inch).

The capsule is connected by a short piece of rubber tubing to a metal cup which is placed in the usual way over the blood vessel from which the pulse tracing is to be made. The membrane on the capsule is made of dental dam or even thinner rubber, depending on the amplitude desired on the tracing. The small mirror is cut from a silvered cover slip 0.006 inch thick and fastened to the membrane with a drop of rubber cement.[3, 4]

Immediately in front of the timer is an adjustable metal shutter which may be set to block off the electrocardiographic light from half the field, so that the heart sounds and pulse tracing appear on the record as black lines on a pure white background. The lower half of the record containing the electrocardiogram has the usual gray background with white time lines (Fig. 5).

There are five units comprising the sound and pulse equipment: the lamp, the prism, the galvanometer, the segment capsule, and the amplifier. Each one is mounted on wedge-shaped dovetail base which fits into a corresponding female part on the table and is held in place by an automatic spring lock. Thus each unit may be easily removed from the electrocardiograph table and quickly put back into its exact working position. The positions of the two lenses and the prism may be adjusted once and clamped firmly so that no further adjustment is necessary. The wedge-shaped mounting blocks, the prism housing, and the segment capsule and its carriage are all made of an aluminum alloy, ST-17, which is light, strong, easily machined, retains a bright finish without plating, and is about half as expensive as unplated brass.

SUMMARY

A simple, compact assembly is described for recording heart sounds and pulse tracings simultaneously with the electrocardiogram.

We are indebted to Dr. Louis N. Katz for his interest and guidance in developing the method.

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Department of Clinical Reports

PRIMARY FIBROSARCOMA OF THE HEART*

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IN 1918, Perlstein,[1] after a search of the literature on the subject, found thirty cases of primary sarcoma of the heart and added one case, but of these only three cases were classified as fibrosarcoma. In 1932 Popp[2] reported an additional case of fibroblastic sarcoma, but examination of Lymburner's collection[3] of 230 cases of primary tumors of the heart, 57 of which were sarcomas, failed to reveal additional cases of fibrosarcoma.

REPORT OF CASE

Baby M. B. was born Oct. 10, 1933, the twelfth child in the family; all the other chidren were living and well and had no anatomical defects. The family history was negative. This boy was born with a complete harelip and cleft palate and at the age of three months a bilateral inguinal hernia appeared. On March 5, 1934, the boy was admitted to the hospital on the service of Dr. Hugh Beatty, for repair of the facial defect. The physical examination on admission revealed a right opening into the oral pharynx, a defect in the right incisura region, and a complete harelip. The faucial and pharyngeal tonsils were not visible. The eyes, ears, neck, heart, and lungs presented no demonstrable abnormality, and there were no adenopathies. Roentgenographic examination showed no abnormal increase in the thymus shadow; the lungs were completely expanded, the trachea was normal in course and outline, and the heart normal, with no visible shadows suggestive of a tumor. The temperature was normal, pulse regular, rate 100, and the body weight was 12 pounds and 7 ounces. The blood count showed 80 per cent of hemoglobin, 4,240,000 erythrocytes, 19,250 leucocytes, with 34 per cent of polymorphonuclear cells and 66 per cent of lymphocytes. The Wassermann and Kahn reactions were negative; the coagulation and the bleeding time and the urine were normal. Cultures of the nose and throat showed no pathogenic organisms.

On March 16, 1934, a Brophy bone operation was done, in which some approximation of the cleft palate borders was obtained with difficulty because of a large amount of calcification of the superior maxillae. On March 29, 1934, the wires were tightened and on May 9, 1934, complete approximation of the cleft palate was obtained. These operations were performed under oxygen-ether anesthesia, and no untoward reaction occurred. On July 12, 1934, the cleft in the upper lip was closed under oxygen-ether anesthesia, but the child reacted badly to this anesthesia during the entire operation, and the respirations were shallow, jerky and arrhythmic. The pulse at the close of the operation was 176, and the temperature 108° F., while immediately before the operation the temperature had been normal. The child died twelve hours after operation.

*From the Pathological and Cardiological Departments of White Cross Hospital, Columbus, Ohio.

Autopsy.—The body was that of a well-developed male white baby, nine months of age, measuring 28 inches in length. The eyes were brown; the hair was light and thin. The jaws were firmly closed by rigor mortis, and the right side of the upper lip had been recently repaired in the process of closure of a harelip. The head was slightly larger than normal, but the contour remained regular and was not of sufficient size to classify as hydrocephalic. The posterior fontanel was completely closed, while the anterior fontanel was large, depressed and calcified only about the margin. There was a marked post-mortem lividity, but no special marks of identification.

Thoracic Cavity: The thymus was not enlarged, being instead somewhat small for a child of this age, and upon removal weighed 9 gm. Both lungs were free, and there was no increase in pleural fluid. The right lung was crepitant but deeply con-

Fig. 1.—The heart at autopsy, showing the dense circumscribed tumor occupying the interventricular septum at the apex, with marginal invasion into the myocardium of the left ventricle.

gested throughout, and in the lower lobe there was what appeared to be an early bronchial pneumonia with a few petechiae over the anterior pleural surface. The left lung was similar, and the trachea and bronchi were free and open. The pericardial sac was smooth and glistening and contained the usual amount of clear fluid. The heart and great vessels were in the normal position, but the heart was elongated, and the apical portion had a peculiar whitish color. The heart weighed 46 gm. and the longitudinal diameter on the anterior surface was 5.5 cm. from the atrial-ventricular groove to the apex. The right ventricle appeared to be somewhat small and measured 25 by 22 mm., and the pulmonary and tricuspid valves were normal, the pulmonary measuring 25 mm. and the tricuspid 45 mm. in circumference, while the myocardium was of the usual thickness. The left ventricular cavity measured 40 by 25 mm.; the mitral and aortic valves were normal, the mitral valve measur-

ing 38 mm. and the aortic 30 mm. in circumference. The foramen ovale was closed, and the ductus arteriosus was obliterated. In the apex of the heart, occupying the position of the interventricular septum and extending into the myocardium of the left ventricle, was a hard whitish mass. This tumor was dense, well circumscribed, measured 22 by 26 mm. and was overlaid by a thin layer of normal myocardium (Fig. 1). The cut surface of the tumor revealed fine interlacing bundles of fibrous tissue without degeneration. No other tumors were found and the coronary arteries were normal. The peritracheal and peribronchial nodes as well as those within the arch of the aorta were moderately hyperplastic.

Abdominal Cavity: The peritoneum, liver, gallbladder, pancreas, spleen, stomach, adrenal glands, and urinary bladder were normal. The mucosa of the duodenum

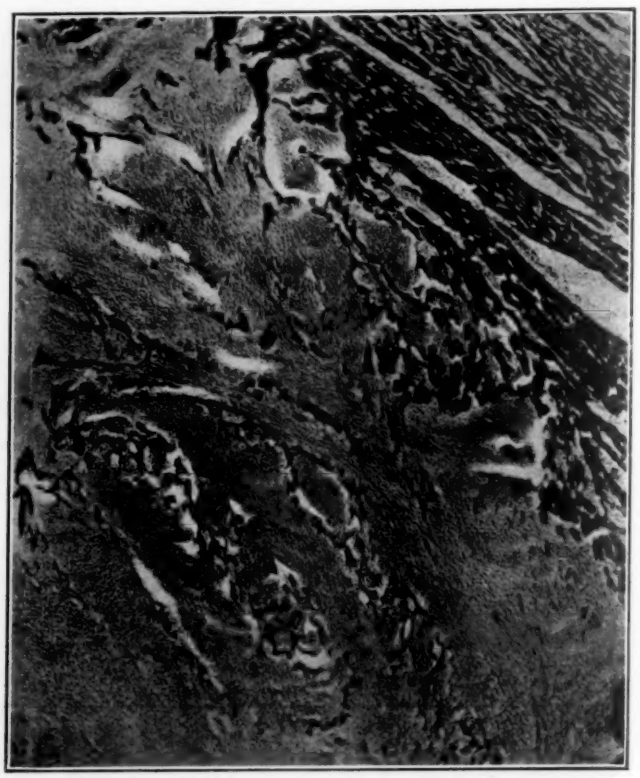

Fig. 2.—Low power photomicrograph showing the marginal invasion of the tumor into the myocardium of the left ventricle and the closely packed fibroblastic cells arranged in broad irregular bundles toward the center of the tumor.

and ileum was studded with small closely set elevations which had the appearance of multiple areas of lymphoid hyperplasia, while the rest of the intestinal tract was normal. The mesenteric lymph nodes were diffusely enlarged and congested; the largest measured 12 by 7 mm. There was a dilatation of the right and left ureters, averaging 4 mm. in diameter, and also a dilatation of the right and left pelves but the kidneys were normal.

Cranial Cavity: The brain and coverings were normal.

Microscopic Examination: There was marked congestion and edema in both lungs but no evidence of pneumonia. There was a marked hyperplasia of the lymphoid tissue of the duodenum in the submucosal layer with displacement out-

ward and erosion of the overlying mucosa. The spleen and kidneys were moderately congested. The mesenteric lymph nodes showed a marked hyperplasia and congestion almost to the point of hemorrhage.

The tumor in the heart was of a poorly circumscribed fibrous type which invaded and replaced the myocardium at the tumor margin (Fig. 2). Sections stained with hematoxylin-eosin, van Gieson, acid fuchsin, phosphotungstic acid-hematoxylin revealed the cells closely packed and of the fibroblastic type, while the cell margins were distinguished with difficulty and the cell nucleus was prominent and elongated. These cells formed broad bundles having a slight tendency to follow the few blood vessels present, but chiefly they were arranged so that longitudinal, cross and oblique sections appeared (Fig. 3). The intracellular stroma was not abundant. The

Fig. 3.—High power photomicrograph of the marginal portion of the tumor showing elongated nuclei of the fibroblastic type with the cell margins indistinct.

rest of the myocardium of the ventricles and auricles was normal, but in the interventricular septum immediately above the tumor there was a fibrosing process similar to that of the tumor but producing fibrous tissue of a more adult type.

Diagnosis: Primary fibrosarcoma of the heart. Generalized lymphoid hyperplasia with exception of the thymus. Congestion and edema of the lungs. Hydronephrosis. Recently repaired harelip and cleft palate.

COMMENT

This localized, fairly circumscribed fibrous tumor originating in the myocardium, probably from the perimesial tissue, growing and extend-

ing by marginal invasion and conversion of the surrounding myocardial cells, and replacing these cells with young fibrous connective tissue cells and later by adult fibrous tissue, is considered by us and others* as a fibrosarcoma.

The case reported by Erickson[4] was in a male thirty-six years old, and the fibrosarcoma was in the left auricle. That of Juergen[5] was in a male thirty-six years old, with a fibrosarcoma in the right auricle. That of Raw[6] was in a female forty-three years old, with the fibrosarcoma in the right auricle, and that of Popp[2] was in a male thirty-three years old, with the fibrosarcoma in the right auricle. The case herein reported is exceptional because the fibrosarcoma was located and confined to the ventricle and appeared in a male only nine months old. It is also unique because the primary sarcomas are not considered to be associated with developmental defects as are the rabdomyomas, whereas associated with this tumor were a harelip, cleft palate, and double inguinal hernia.

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*Dr. L. J. Rhea and Dr. Maude Abbott, Montreal, Canada, who examined the sections.

ACUTE CORONARY THROMBOSIS AND MYOCARDIAL INFARCTION AFFECTING A PATIENT THIRTY-ONE YEARS OF AGE*

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WE HAVE been accustomed to think of acute coronary occlusion with myocardial infarction as mainly affecting individuals past forty years of age, and certainly in the majority of instances this impression is correct. The number of patients less than forty years of age who have died of acute coronary occlusion, which was proved by necropsy, is relatively small. Up to 1932, twenty proved cases and ten questionable cases had been reported in the literature. Before the characteristic electrocardiographic findings of acute myocardial infarction were well understood, it was difficult to be absolutely sure of the clinical diagnosis of acute coronary occlusion. With the advent of this electrocardiographic knowledge, the diagnosis of acute coronary occlusion and myocardial infarction can be made with higher degrees of certainty. Before we had the aid of the electrocardiograph, the diagnosis of acute coronary occlusion which affected young individuals had to be made with considerable reservations, but with its aid the diagnosis can now be definitely established without necropsy. Because of the extreme rarity of acute coronary occlusion among individuals who are in their early thirties, we are reporting a case in which the patient was thirty-one years of age.

REPORT OF CASE

When twenty-six years of age (1931) the patient had been refused a life insurance policy because of hypertension. During the succeeding five years the blood pressure had been taken, and urinalysis had been performed every few months by his home physician. The value for the systolic blood pressure had varied from 140 to 200 mm. of mercury. Albumin had been constantly present in the urine for three years before he came to the clinic. Subjectively, he had remained well until August, 1936, at which time he was thirty-one years and nine months of age.

In August, 1936, he had begun to note retrosternal distress after unusual exertion. Rest had afforded prompt relief. The symptom had progressed rapidly and had become associated with a numb feeling in the left arm, and, later, in both arms. Within a month he could not walk a single block without anginal pain. By October, 1936, even the exertion of dressing would produce the characteristic distress. When we first saw him, in November, 1936, he said that it took an hour and a half to dress and that he could walk only at the slowest pace, with frequent rests. He had severe, even violent, retrosternal pain. The pain was associated with numbness in both arms, which was maximal in the left anterior cubital fossa. Complete rest caused relief

*From the Section on Cardiology and the Division of Medicine of the Mayo Clinic.

within a few seconds or minutes. At one time he had had a pain that had been a great deal more severe than any other pain he had ever experienced, but this pain had not lasted longer than fifteen or twenty minutes and it had not been accompanied by shock or other symptoms which are usually associated with myocardial infarction. His tolerance for exercise had been decreased after this severe attack of pain, and each week thereafter he had seen a definite progression of the symptoms.

Physical examination revealed a well-looking young man who was very intelligent and cooperative. The value for the systolic blood pressure varied between 160 and 180 mm. of mercury. No other objective evidence of organic disease was detected by physical examination. Funduscopic examination showed a moderate degree of generalized narrowing of the retinal arteries without evident sclerosis or retinitis. Roentgenological examination of the thorax revealed a heart shadow that was well within normal limits. The urine contained moderate amounts of albumin (grade 2), and one specimen contained a few erythrocytes. An electrocardiogram, which was taken in September, a few days after the most severe attack of pain, showed an inversion of the T-wave and a change of contour of the S-T segment in Lead I, an exaggeration of the T-wave in Lead III, a positive T-wave in Lead IV (Wolferth), and an absence of the Q-wave in Lead IV. In view of these findings and the fact that an electrocardiogram taken about two months later revealed an essentially normal tracing, we have almost positive proof that the patient had an acute coronary occlusion with myocardial infarction.

COMMENT

This patient is of interest because he is only thirty-one years of age. He recovered from his acute myocardial infarction, but following the infarction a very severe progressive angina pectoris developed. Because of this, we believe the prognosis is very bad.

Department of Reviews and Abstracts

Selected Abstracts

Johnson, J. Raymond, and Wiggers, Carl J.: The Alleged Validity of Coronary Sinus Outflow as a Criterion of Coronary Reactions. Am. J. Physiol. 118: 38, 1937.

By recording the velocity of coronary sinus flow, returned at once to the superior vena cava, and by calculating the flow per beat and per minute, it was found that: 1, the coronary sinus normally empties into the atrium only during systole; 2, increasing the right ventricular pressure by compression of the pulmonary artery—the heart rate and aortic pressures remaining the same—causes a proportional augmentation of coronary sinus flow; 3, the increase in minute flow following only slight elevation of systolic right ventricular pressure is of the same order of magnitude as that frequently reported from stimulation of cardiac nerves or actions of drugs.

A theory is presented and supported by experiments that the division of coronary return flow between coronary sinus and thebesian veins is determined not only by the anatomical resistance of these respective paths, but by the height to which right ventricular pressure rises during each systole. This accounts for the proportionally larger flow from the coronary sinus in normally beating hearts and the greater drainage by thebesian vessels in dead hearts. It proves that a greater coronary sinus flow can occur through secondary increase in right ventricular pressure alone.

The conclusion is reached that inferences regarding vasomotor actions in the coronary system based on alterations in coronary sinus outflow cannot be accepted as crucial unless it is demonstrated that right ventricular systolic pressure remained unchanged.

AUTHOR.

Moore, Robert M., and Greenberg, Max M.: Acid Production in the Functioning Heart Under Conditions of Ischemia and of Congestion. Am. J. Physiol. 118: 217, 1937.

Both coronary arterial trunks were ligated in anesthetized cats. The heart became pale, and after a few minutes there were reflex signs of a stimulation of pain elements. In many experiments ventricular fibrillation ensued. In every case the ventricles became widely dilated within ten minutes after ligation of the arteries. After a period of ischemia varying from three to nine minutes, a sample of blood was taken from a coronary vein and a control sample from the vena cava. The coronary venous blood showed a marked lowering of pH, whereas its lactic acid content was increased greatly. The actual fall in pH, as indicated by comparison with blood from the vena cava, varied from 0.22 to 0.81. It exceeded 0.50 in nine of eighteen cats. In three animals the pH of the coronary blood fell below 6.6, and in one animal it reached 6.40. These pH values, we believe the lowest ever reported for blood from the living animal, illustrate how rapidly acid metabolites accumulate when functioning tissues are isolated from the arterial circulation.

Identical experiments were performed upon five dogs with results similar to those obtained in the cat.

In a separate series of cats all the major cardiac veins were ligated to produce venous congestion. Although the heart became markedly congested and its surface "wept" from transudation, the lowering of the pH of the coronary venous blood was so slight as to be questionable, and there was only a small change in the lactic acid content. After twenty or thirty minutes of congestion the heart continued to perform its function in an apparently normal manner.

Under the conditions of the experiments the lowering of the pH of the coronary venous blood to 6.6 or below after a few minutes of ischemia indicates a much greater acid change in the cardiac muscle. The significance of this chemical alteration is discussed with reference to the occurrence of pain in ischemic lesions of the heart and of the extremities. In view of the sensitivity of pain endings to acid (Moore, Moore, and Singleton, 1934), it is concluded that in such clinical cases the accumulation of acid metabolites in the area devoid of arterial circulation can well be of a magnitude to account for the pain.

AUTHOR.

Shipley, R. A., Shipley, Louise J., and Wearn, Joseph T.: The Capillary Supply in Normal and Hypertrophied Hearts of Rabbits. J. Exper. Med. 65: 29, 1937.

During normal growth of the rabbit heart, muscle fibers enlarge, and the capillaries multiply so that a relatively constant capillary supply per unit of tissue is maintained from the time of birth to maturity.

In cardiac hypertrophy the muscle fibers enlarge, but the capillaries do not multiply, and, as a result, the capillary supply per unit of tissue is reduced.

The decreased concentration of capillaries in the hypertrophied heart would constitute an impediment to the adequate exchange of metabolic substances, but the seriousness of the impediment cannot be estimated without further physiological data.

AUTHOR.

Marcu, J.: The Genesis of Embryonic Heart Action on the Basis of a Hydraulic Tube Phenomenon. Klin. Wchnschr. 15: 600, 1936.

The author noted that, when a continuous stream passes through an elastic rubber membrane, it becomes converted into an intermittent stream. He attributes the beating of the embryonic heart to a similar phenomenon.

L. N. K.

Schoedel, W.: Action of Vasodilator Substances on the Work and Blood Flow of Active Skeletal Muscles. Pflügers Arch. f. d. ges. Physiol. 237: 190, 1936.

The author found that vasodilators, like histamine, acetylcholine, adenosine, and muscle adenylic acid, did not improve muscle contraction.

L. N. K.

Paschkis, K.: Anemia and Anoxemia of the Heart Muscle—An Experimental Investigation of Angina Pectoris. Wien. Arch. f. inn. Med. 28: 447, 1936.

In rabbits small doses of adrenalin cause no electrocardiographic changes. The same doses cause changes in the T-wave, however, if the animal is made anemic. The adrenalin by increasing O_2 metabolism of the heart summates with anemia to cause anoxemia in the heart muscle.

L. N. K.

Halbsgut, A.: Action of Extracts of Bulbus Scillae and Scillaren on the Conduction System and Refractory Phase of the Frog's Heart. Klin. Wchnschr. 15: 420, 1936.

The author finds that the heart rate and conduction rate are slowed, systole is lengthened, and the refractory phase is lengthened. The heart eventually goes into a systolic standstill.

L. N. K.

Wood, Francis Clark, and Wolferth, Charles Christian: The Tolerance of Certain Cardiac Patients for Various Recumbent Positions (Trepopnea). Am. J. M. Sc. 193: 354, 1937.

Certain cardiac patients who are able to lie comfortably in one recumbent position cannot tolerate another.

They usually prefer the right side and dislike the left, but there are many variations.

Dyspnea and precordial discomfort are the most common symptoms which are experienced in one horizontal position and relieved on the assumption of another. Cough and anginal pain are less relieved by assuming another. Cough and anginal pain are less frequent. Fatigue, dizziness, and palpitation are also described. These are the same symptoms which lead an orthopneic patient to sit up.

Patients with this syndrome usually show considerable cardiac enlargement and definite reduction in cardiac functional capacity. The symptoms may change in intensity as the clinical condition of the patient changes. There is no apparent correlation between the position the patient prefers and any known cardiovascular characteristic, such as type of lesion, type of failure, or shape of heart.

Observation of patients in their unfavorable recumbent positions shows that their complaint of dyspnea is probably subjective phenomenon, a sense of suffocation, which may or may not be accompanied by obvious increase in rate or depth of breathing. This is also true of orthopnea.

Roentgenological study shows that the heart may move considerably as a patient changes from one side to the other; that the intensity of symptoms is not proportional to the distance the heart moves; that the shape of the heart and aortic arch may change markedly as the subject changes position; and that, with the patient in lateral decubitus, the heart is lifted during each inspiration, sometimes a distance of several centimeters.

The vital capacity does not tend to be greater in the most favorable recumbent position than in the most unfavorable one.

Patients in whom this phenomenon is marked do not assume their most unfavorable position at night, even when asleep. Those in whom it is less well developed are sometimes found in an unfavorable recumbent position during sleep, although they may deny that they can tolerate this position.

Observations of the pulse, the arterial pressure, the cervical veins, and the heart sounds have not as yet been productive of helpful information.

Electrocardiographic tracings have failed to show a change in an unfavorable position which can be attributed confidently to a change in cardiac action.

One subject without heart disease or preference for any particular recumbent position showed a lower cardiac output when lying on the left side than on the right.

Change of position of the heart with distortion of the large vascular channels in the mediastinum is suggested as a possible cause for this phenomenon. The venous return from the lungs might readily be obstructed by this mechanism.

These observations may help to explain the mechanism of production of orthopnea and paroxysmal noctural dyspnea.

This phenomenon has been named "trepopnea" for the sake of brevity, even though it does not express the concept adequately.

AUTHOR.

Sampson, John J.: Study of Depth Temperatures in Artificial Fevers and Cooling Air Chambers With Especial Reference to Cooling Effect of the Circulating Blood. Am. J. Physiol. **117**: 708, 1936.

Temperature determinations of skin surfaces, deep skin, subcutaneous tissue, muscles, and blood in the precubital veins were made on normal individuals and on normally afebrile patients undergoing artificial fever treatments. Such observations were made under normal circumstances, at various stages of the fever production, by (1) intravenous vaccine, (2) the "blanket pack" method alone, and (3) the "blanket pack" preceded by heating in an electric light cabinet. Observations were made likewise on such individuals during cooling by surface sponging and by inspiration of iced air. Individuals with normal temperature were likewise studied under the influence of cooled air inhalation.

The recognized gradients between the deep tissue and surface skin were observed with the exception that occasionally the skin was warmer than the subcutaneous tissue under normal circumstances. This phenomenon generally occurred during artificial fever with the "blanket pack" method. The behavior of the intravenous blood temperature under various circumstances leads to the conclusion that the blood may serve as an important cooling agent to the general body tissues, losing more heat in the respiratory tract than has been believed heretofore.

AUTHOR.

Goldsmith, Grace: Cardiac Output in Polycythaemia Vera. Arch. Int. Med. **58**: 1041, 1936.

Determinations of the cardiac output and detailed studies of the blood have been carried out over a period of eight months in a case of polycythemia vera. The cardiac output, which was elevated considerably above normal prior to the institution of treatment, decreased as certain hematologic values approached normal. The increase in the basal metabolic rate in this case does not entirely explain the increased cardiac output. It is suggested that the increased volume of blood may be a factor in this regard. Another factor may be the decreased percentage of plasma per unit of blood, causing a deficiency in the transportation of nutrient substances to the tissue. The cardiac output in three additional cases of polycythemia vera is reported; in two the findings were within normal limits; and in one there was a slight elevation of the output. Two of these patients were followed during treatment, and it was observed that the cardiac output tended to decrease as the blood picture approached normal.

AUTHOR.

Spink, Wesley W.: Pathogenesis of Erythema Nodosum, With Special Reference to Tuberculosis, Streptococcic Infection, and Rheumatic Fever. Arch. Int. Med. **59**: 65, 1937.

Ten patients with erythema nodosum were critically studied.

No evidence of tuberculosis was present, except in one patient.

The following data indicate a causal relationship between *Str. hemolyticus* and erythema nodosum: In five of the ten patients a sore throat preceded erythema nodosum, and cultures in four cases revealed *Str. hemolyticus* of the beta type; intradermal injection of a streptococcus endotoxin (nucleoprotein) produced nodules

similar to the lesions of erythema nodosum in eight of the ten patients; excised streptococcic nodules and the lesions of erythema nodosum revealed the same histologic appearance; similar lesions were produced by the injection of broth filtrates of streptococci isolated from two of the patients. The same picture has been produced by the injection of tuberculin.

An analysis of the records of 133 patients treated for erythema nodosum at the Boston City Hospital from 1924 to 1934 revealed a similar causal relationship to streptococcic infections and, in addition, to rheumatic fever.

A general review of the literature is presented.

Erythema nodosum appears to be a nonspecific inflammatory reaction of the skin to a variety of bacterial, toxic, and chemical agents.

AUTHOR.

Coburn, Alvin F., and Moore, Lucile V.: Experimental Induction of Erythema Nodosum. J. Clin. Investigation **15**: 509, 1936.

The intracutaneous injection of the appropriate antigen in a patient with subsiding erythema nodosum is regularly followed by an intense inflammatory reaction at the site of injection.

The development of this local reaction was followed in half of the subjects tested by a recrudescence of erythema nodosum in the areas recently affected.

The capacity of the involved extremities to develop erythema nodosum persisted for only a few weeks.

A possible relation between the induction of erythema nodosum and an antigen-antibody reaction is discussed.

AUTHOR.

Gibson, John G., and Evans, William A., Jr.: Clinical Studies of the Blood Volume: I. Clinical Application of a Method Employing the Blue Azo Dye "Evans Blue" and the Spectrophotometer. J. Clin. Investigation **16**: 301, 1937.

The application of a method for determining the plasma and total blood volume employing the blue dye, Evans blue, and the spectrophotometer to the investigation of clinical problems is described.

Colorimetric errors inherent in earlier methods due to turbidity of plasma, lipemia, residual dye in repeated determinations, and hemolysis of samples are minimized by the use of the spectrophotometer, and a spectrophotometric method of correcting for hemolysis is described.

Errors due to variations in dye mixing time occurring in different clinical states, and possible dilution of injected dye by lymph are eliminated by calculating the plasma volume from a value obtained by extrapolation of the slope or disappearance of the dye from the blood stream, as determined by multiple samples taken over a period of at least thirty minutes after dye injection, to the time of injection.

By the "direct" method of repeated single determinations, volume changes of clinical significance in the same individual can be reliably measured at frequent intervals. By the "indirect method" changes in volume can be continuously followed for periods of from a few minutes to several hours.

Certain factors affecting the accuracy of the indirect method are discussed. A physiological response to serial blood sampling, consisting of a transient and variable decrease in the circulating plasma and red cell volume, renders accurate estimation

of the rate of disappearance of dye from the blood stream difficult. Experimental procedures may alter the intrinsic color of the serum and rate of dye disappearance.

AUTHOR.

Gibson, John G., and Evans, William A., Jr.: Clinical Studies of the Blood Volume: II. The Relation of Plasma and Total Blood Volume to Venous Pressure, Blood Velocity Rate, Physical Measurements, Age and Sex in 90 Normal Humans. J. Clin. Investigation **16**: 317, 1937.

Plasma and total blood volumes, venous pressures, and blood velocity rates were determined in 49 normal males and 41 normal females.

No relationship exists in normal persons between variations in total blood volume, venous pressure, and blood velocity rate.

The total blood volume of normal males is greater than that of females, the difference being due to the greater red cell volume of males. The absolute red cell volume of females is less than that of males by a much greater degree than indicated by differences in red cell counts and hematocrit values.

With increasing age there is a decline in the blood volume comparable to decreases in basal metabolic rates and vital capacities.

In comparison to average values, the absolute total blood volume is high in muscular and obese persons and low in thin individuals; the volume per unit of body weight is high in muscular and in thin individuals and low in obese persons.

The blood volume of normal individuals varies within wide limits. The relationship to height or surface area offers a useful basis for estimation of normal volume in clinical investigation.

AUTHOR.

Gotsev, T.: Action of Acetylcholine on Blood Vessels, Blood Pressure, Heart and Vasomotor Centers. Arch. f. Exper. Path. u. Pharmakol. **181**: 207, 1936.

The author attributes a drop in blood pressure to a slowing and a depression of the heart, since atropine causes the blood pressure to rise and the heart to accelerate. The volume of the viscera decreases, as a rule, whether the blood pressure rises or falls.

L. N. K.

Grosse-Brockhoff, F., Schneider, M., and Schoedel, W.: Vasomotor Interference in the Nerve Plexus of Skeletal Muscle Vessels Induced by Vasodilator Substances Following Hyperemia. Pflüger's Arch. f. d. ges. Physiol. **237**: 178, 1936.

In local hyperemia in the skeletal muscle induced by acetylcholine, the authors find an absence of normal vasoconstrictor action of the carotid sinus and of small adrenalin injections. This refractoriness resembles the effect found in hyperemia following activity, and this refractoriness is absent when histamine, adenosine, or muscle adenylic acid is used. In fact, the response to small doses of adrenalin is exaggerated under the latter conditions.

L. N. K.

Roeske: Movements of Lower Lung Margin and Apex Beat on Lying Down and Sitting Up. Deutsche med. Wchnschr. **62**: 542, 1936.

Movements are due to changes in position of the anterior chest wall in these two positions. The lower lung margin follows the chest, but the heart does not. Hence

with the subject lying down the lung margin moves down and the apex beat up. The movements of the anterior chest wall can be easily demonstrated by palpitation of the ribs.

L. N. K.

Herbst, R., and Manigold, K.: Circulatory Insufficiency and O_2 Deficiency. Ztschr. f. klin. Med. **129**: 710, 1936.

The effect of the low pressure chamber on compensated and decompensated cardiac patients (valvular deformities, hypertension, emphysema, and coronary sclerosis) was determined. The response of patients with compensated hearts to lowering of pressure is the same as in normal subjects. In patients with decompensated hearts the onset of mountain sickness occurred at lower elevations, viz., 1 to 2 kilometers instead of 3.7 kilometers. Even at elevation lower than this an acceleration of the pulse and increased minute volume blood flow were noted. Before collapse occurred, the minute volume flow decreased.

L. N. K.

Block, C.: Extrasystolic Allorhythmia. Wien. Arch. f. inn. Med. **28**: 55, 1936.

A case of old coronary occlusion is described in which there were A-V and intraventricular block and spontaneous allorhythmia. Each effective normal sinus beat was followed by a series of ventricular extrasystoles which interfered with the sinus rhythms. The changes in cycle length of the succeeding extrasystoles were ascribed to "exit" block which usually caused the second impulse to be blocked out. In larger runs of extrasystoles others were blocked out also.

L. N. K.

Neslin, W.: An Autonomic Auricular Rhythm. Wien. Arch. f. inn. Med. **28**: 243, 1936.

A rhythm independent of sinus rhythm occurred in the auricles. The pacemaker affected only a part of the auricles and was blocked from the ventricle and sinus node. The author believes this to be an instance of complete persistent intra-auricular block.

L. N. K.

Block, C., and Pick, A.: Action of Magnesium on Ventricular Ectopic Rhythms Occurring in Digitalis Intoxication—III. Wien. Arch. f. inn. Med. **29**: 435, 1936.

A case is described of auricular fibrillation with rapid ventricular rate. A 20 per cent solution of $MgSO_4$ caused ventricular slowing by producing an A-V block. The maximum effect lasted from five to fifteen minutes, but the action persisted for some time.

L. N. K.

Knoll, W., Girones, L., and Goerke, W.: Time Relation Between Heart Activity and the Electrocardiogram. Deutsche. med. Wchnschr. **62**: 140, 1936.

Each electrocardiogram of an exposed heart, in a dog and in a monkey, was recorded simultaneously with the cinematograph. It was found that QRS occurs when the heart is dilating and T while the ventricle is contracting in size.

L. N. K.

Frey, H.: The Efficiency of Various Electrocardiographs. Ztschr. f. Kreislaufforsch. **29**: 41, 1937.

An ideal instrument should (1) register accurately at all vibration frequencies found in the electrocardiogram, (2) give proportional responses to all imposed stresses regardless of magnitude or direction, (3) cause no phasic distortion, (4) cause no alterations in potential at lead-off point, (5) be easily transportable, and (6) be easy to operate. The author discusses the various instruments on this basis. He concludes that the string galvanometer is not suitable for chest leads because of polarization. [This argument is not convincing.] The author believes that a constant potential amplifier and a cathode ray oscillograph when properly constructed are best. The alternating potential amplifier must have a time constant of at least 1 to 1.5 sec. if it is to be used. Moving coil oscillographs require an inherent vibration frequency of 600 to 1,000.

L. N. K.

Pick, A.: Concerning Atypical Bundle-Branch Block. Ztschr. f. klin. Med. **129**: 719, 1936.

The author presents twenty-four cases of advanced intraventricular block, all of which showed a prolongation of the second phase of the QRS complex, the first phase being normal in duration or only slightly prolonged; and the T-wave was opposite in direction to the prolonged phase of QRS.

The prognosis in this group is similar to other groups of intraventricular block. The commonest cause of this condition was arteriosclerosis. A necropsied case is described, showing the transformation of an atypical to uncommon type of intraventricular block following myocardial infarction. This indicates that other conditions besides the location of the block help to determine the electrocardiographic appearance in man.

L. N. K.

Schlomka, G., and Gauss, G.: Clinical Electrocardiography: IV. Observations in Emphysema. Ztschr. f. klin. Med. **129**: 760, 1936.

One hundred patients with emphysema were studied. The authors found a tendency toward right axis shift. The degree of this is related to severity of lung involvement.

L. N. K.

Langendorf, R., and Pick, A.: Electrocardiogram in Lung Embolism. Acta med. Scandinav. **90**: 289, 1936.

Four necropsied cases of lung emboli showing marked electrocardiographic changes are described. No abnormalities in the heart or the coronary arteries were found to explain the changes. The authors found a total of 12 out of 16 cases in the literature which showed electrocardiographic changes in the first twenty-four hours typical of localized myocardial ischemia usually resembling posterior infarct. This does not run a typical course, however, in seriatum curves.

L. N. K.

Parade, G. W.: Heart Arrhythmias Following Mental and Physical Trauma. Med. Klin. **32**: 733, 1936.

Two cases of auricular fibrillation are reported. In one case a healthy athlete developed a paroxysmal auricular fibrillation of several hours' duration during underwater swimming. In the second case an emotional but healthy man developed a similar paroxysm of several days' duration which was initiated by rage.

L. N. K.

Langendorf, R., and Pick, A.: Electrocardiogram in Acute Nephritis. Med. Klin. **33**: 126, 1937.

In twelve cases of acute diffuse glomerulonephritis the authors found typical changes as illustrated in three cases described in detail.

The records must be distinguished from the curves seen in pericarditis and anterior wall infarction. The changes are ascribed to sudden elevation in blood pressure and presumably ischemia and inflammatory or toxic factors.

L. N. K.

Bischoff: A Case of Heart-Block (the Roentgenokymographic and Electrocardiographic Findings). Klin. Wchnschr. **15**: 702, 1936.

A case of complete A-V block in a seventy-year-old man with ventricular rate of 20 and an abnormal QRST with widened QRS is presented. No evidence of heart failure was present, and the cerebral blood flow seemed adequate at rest and on slight exertion. The disorder could be identified on kymography.

L. N. K.

Rothberger, C. J., and Zwillinger, L.: Action of Magnesium on Strophanthin and Barium Tachycardia. Arch. f. exper. Path. u. Pharmakol. **181**: 301, 1936.

The authors found that magnesium depressed the ectopic pacemakers in animals and made it more difficult to induce strophanthin and barium tachycardia. This explains the action of magnesium clinically in abolishing extrasystoles and paroxysmal tachycardia. The quantities of magnesium required in anesthetized animals is greater than in man.

L. N. K.

Eckey, P.: Unusual Effects of Small Doses of Strophanthin on Rhythmicity and Conductivity of the Heart and Its Relation to Parasystole. Deutsches Arch. f. klin. Med. **178**: 652, 1936.

In one case, three intravenous injections of 0.3 mg. of strophanthin caused a parasystole. In a second case two injections intravenously of 0.3 mg. each caused A-V block with dropped beats and Wenckebach periods. In a third case there was a prolongation of the P-R interval abolished by atropine and hence attributed to a vagus action.

L. N. K.

Schwartz, Sidney P.: Studies on Transient Ventricular Fibrillation: IV. Observations on the Clinical and Graphic Manifestations Following the Revival of the Heart From Transient Ventricular Fibrillation. Am. J. M. Sc. **192**: 808, 1936.

Correlated observations were made of the clinical and graphic manifestations following the spontaneous revival of the heart from transient ventricular fibrillation in seven patients with either transient or established A-V dissociation.

It was determined that revival of the heart from transient ventricular fibrillation in man is associated usually with a postfibrillatory pause, followed by a variable standstill of the ventricles and an intermediary idioventricular rhythm with a progressive increase in the heart rate to as high as 160 beats per minute before the restoration of the basic ventricular rhythm.

The duration of this postfibrillatory period is dependent upon the duration of the antecedent period of ventricular fibrillation and is independent of the type of ventricular oscillations present during the fibrillatory period. It may vary from a few seconds to as long as one-half hour at one time.

The spontaneous revival of the heart from transient ventricular fibrillation is associated clinically with a sudden flushing of the face and entire skin by a pink-red coloration, a forceful pulsation of the heart against the chest wall, and a barely perceptible beat of the pulse at the wrist. With these events the eyes are opened, and loud screaming may be followed by incoherent and unintelligible speech, a very cloudy sensorium, and a progressive increase in the heart rate as noted from the electrocardiograms. This in turn is followed by a progressive lowering of the heart rate again to the original basic level prior to that present before the onset of ventricular fibrillation. Coma and a period of unconsciousness may then supervene and last as long as five hours after a major syncopal attack.

The period of apnea present during ventricular fibrillation is replaced at first by irregular periods of respirations in which inspiration is prolonged. There may then appear typical Cheyne-Stokes respirations as well as all forms of irregular respiratory movements noted after asphyxia.

Occasionally after repeated attacks there is a generalized anasarca, involving the face, the arms, and the entire skin.

All of these symptoms and signs are so unique that a clinical diagnosis of transient ventricular fibrillation may be suspected in an individual with syncopal seizures if they are noted after the attack.

Since the natural course of the revival of the heart from transient ventricular fibrillation includes a period of acceleration of the heart following a postfibrillatory standstill of the ventricles, it is a fallacy to assume that any drug administered during the postfibrillatory period is responsible for the successive events which appear after its use.

AUTHOR.

de Châtel, A.: An Analysis of the Pathological Changes in the S-T Segment and the T-Wave of the Electrocardiogram on the Basis of Direct Leads. II. Ztschr. f. d. ges. exper. Med. **98**: 389, 1936.

The author indicates that the S-T and T changes following coronary ligation, monoiodoacetic acid, NaF, and hemorrhage are due to changes in the electronegativity of certain regions of the ventricles. In coronary ligation the anoxia causes an earlier activation of the region affected. In the more generalized anoxias the anterior wall of the base of the heart is activated earliest. [This is not convincing.]

L. N. K.

Cossio, P., Lascalea, M., and Fongi, E. G.: Alternation of the Heart Sounds. Arch. Int. Med. **58**: 812, 1936.

In seven cases in which different degrees of pulsus alternans were present, the graphic record of the heart sounds showed alternation of the first sound in all cases and alternation of the second sound in only four cases.

The alternation of the first sound was concordant in all cases with the alternation of the pulse beats. In one case only it coexisted and was concordant with an alternation of the T-wave in the electrocardiogram. In another case it coexisted and was discordant with an alternation of the QRS complex.

Alternation of the second sound was concordant with alternation of pulse beats in one case and discordant in three cases. The discordance between alternation of the second heart sound and the pulse beats is associated with its transmissibility from the site where it originates to the place where it is heard in the precordium.

Deliberate precordial auscultation and a mental image of the way the alternation of sounds is perceived enabled recognition of the alternation in all cases. In two

of four cases in which alternation of the first and of the second sound was present, the alternation of the first sound was perceived easier than that of the second sound.

Alternation of the sounds is detected by means of auscultation by the slight differences in the intensity, pitch, and sound that the same sound shows in two successive cardiac cycles. In certain cases there may be a slight typical change in cadence, namely, of the rhythm of their succession.

AUTHOR.

Polanco, Mario: The Relation of Coronary Sclerosis to Symptoms and Its Distribution in 242 Fatal Cases. Am. J. Med. Sc. **192**: 840, 1936.

Study was made of 242 consecutive cases with hearts whose coronary arteries were found postmortem to be sclerotic. There were 156 males (64.5 per cent) and 86 females (35.5 per cent).

History of pain of cardiac origin was given in 14.9 per cent of the cases, of which 24 were males and 13 females; 91.7 per cent of these were associated with marked sclerosis and 8.3 per cent with moderate sclerosis. No cases with mild sclerosis gave a history of pain.

Dyspnea and cardiac pain were the symptoms most frequently encountered. Signs of congestive heart failure were also predominant; of the arrhythmias, auricular fibrillation was the most common, and extrasystole, frequent.

The anterior descending branch of the left coronary artery was the most frequent to be "markedly" involved in the sclerotic process (eighteen times).

Of arteriosclerosis in other organs, the kidneys and spleen were more markedly attacked. Other organs were involved in varying degrees, showing that visceral arteriosclerosis tends to be generalized, although usually affecting the vessels of some organs more than others.

The ratio of heart weight to body weight was found to be increased in 90.8 per cent of the males and 91.3 per cent of the females. The average heart weight in 149 males was 417 gm., or 123 gm. (42 per cent) above normal. Of these, 84 per cent weighed more than normal. Of 78 females, the average weight was 387 gm., or 137 gm. (55 per cent) above normal; 83.3 per cent showed definite increase of heart weight.

AUTHOR.

Baumann, E.: Endocarditis Lenta. München. med. Wchnschr. **83**: 469, 1936.

The author reports forty-three cases of this disease with positive blood cultures of *Streptococcus viridans*. In only one case was an apparent cure induced by neosalvarsan. Other procedures in this series were without avail.

L. N. K.

Kraiss, H.: Recovery in Endocarditis Lenta. Med. Klin. **22**: 566, 1936.

A case of endocarditis lenta with possible recovery (or intermission) of two years' duration is presented. The possibility is considered that a pneumonia from which the patient recovered might have been responsible for the apparent cure.

L. N. K.

Hermann, K.: Pericardial Concretion. München. med. Wchnschr. **83**: 889, 1936.

The signs of congestion are due not only to heart failure but to constriction of the veins entering the pericardium. Surgery gives excellent results.

L. N. K.

Bedford, D. Evan, and Parkinson, John: Right-Sided Aortic Arch. Brit. J. Radiol. **9**: 776, 1936.

Right-sided aortic arch is a congenital malformation of the aorta due to an abnormal evolution of the embryonic arterial arches. Two anatomical varieties are recognized. It may be an isolated anomaly or may be combined with congenital malformation of the heart, especially with Fallot's tetralogy. Eleven cases of right-sided aortic arch are described, and their radiological features are discussed.

AUTHOR.

Taussig, Helen B.: The Clinical and Pathological Findings in Congenital Malformations of the Heart Due to Defective Development of the Right Ventricle Associated With Tricuspid Atresia or Hypoplasia. Bull. Johns Hopkins Hosp. **59**: 435, 1936.

The central feature in this congenital malformation is the diminutive size of the right ventricle. The associated malformations can be postulated from the fact that the right ventricle does not function. The failure of the ventricle to function means that neither the tricuspid valve nor the pulmonary valve can function, and hence they are either atresic or markedly hypoplastic. Furthermore, it means that the only way for the blood to escape from the right auricle is through some defect in the interauricular septum. The extent of this defect determines whether the heart functions as a biloculate or a triloculate heart.

Clinically, the malformation is associated with persistent cyanosis and no murmurs. The diagnosis is established through the recognition of the diminutive size of the right ventricle. This condition can be recognized in the roentgenogram by the peculiar outline of the cardiac shadow. In the anteroposterior view, because of the absence of the pulmonary conus, the upper contour of the cardiac shadow immediately to the left of the sternum has a concave instead of a convex outline. In the left anterior oblique position the small size of the right ventricle is indicated by the absence of cardiac shadow anterior to that of the aorta. These observations are substantiated by the electrocardiogram which shows a left axis deviation.

The differentiation between a functionally biloculate and a triloculate heart depends upon the size of the interauricular septal defect. If there is free communication between the two auricles, i.e., functionally a biloculate heart, physical examination yields no additional positive findings. In contrast, when the interauricular septum is well formed, it causes obstruction to the outflow of blood from the right auricle. Under these circumstances, the auricular pulsation is transmitted to the liver and is readily palpable at its margin. It is this pulsation at the edge of the liver occurring in conjunction with a diminutive right ventricle which distinguishes a functionally triloculate from a functionally biloculate heart.

AUTHOR.

Coburn, Alvin F.: Specific and Non-Specific Changes in Blood Protein During Acute Rheumatism With Carditis. Internat. Clin. **4**: 49, 1936.

Patients with rheumatic carditis show measurable changes in the proteins of the blood, both specific and nonspecific in character. These changes begin at the onset of the rheumatic attack. The nonspecific reaction (increase in the erythrocyte sedimentation rate) reaches its maximum level early in the course of the attack while electrocardiographic abnormalities are most marked. Specific changes (increase in titer of antibody to hemolytic streptococcus) can be detected at the beginning of

the attack but do not reach their maximum level until the nonspecific changes and symptoms are regressing. These relations are characteristic of acute rheumatism irrespective of whether the patient is having the initial attack or a subsequent recrudescence after a year or more of good health. In contrast, failing an antistreptolysin response to hemolytic streptococcus, the rheumatic subject does not develop an attack, and the sedimentation rate remains normal. This indicates that an antistreptolysin response is essential to the development of both the clinical symptoms and abnormal sedimentation rates. The relatively late development of the increase in titratable antibody as compared with the increase in sedimentation rate is a constant characteristic of the rheumatic attack. Its significance will be dealt with in a forthcoming communication.

AUTHOR.

Coburn, Alvin F., and Kapp, E. M.: Observations on the Development of the High Blood Sedimentation Rate in Rheumatic Carditis. J. Clin. Investigation **15**: 715, 1936.

In acute rheumatism, the sedimentation rate may be considered as a measure of the extent of inflammation.

The increased sedimentation rate in acute rheumatism is caused by an increase in plasma fibrinogen and globulin.

An immunological test for a qualitative difference between the plasma protein fractions of normal and rheumatic individuals gave negative results.

A possible type of mechanism is suggested to account for the rise in sedimentation rate just before the onset of a rheumatic attack.

AUTHOR.

Coburn, Alvin F.: Observations on the Mechanism of Rheumatic Fever. Lancet **2**: 1025, 1936.

It becomes increasingly clear that the immune response to hemolytic streptococcus infection is intimately connected with the development of rheumatic activity. Variations in the clinical character of the attack show a close parallel to the types of antistreptolysin curves developed. Up to the present time there has been no evidence as to whether the antistreptolysin curves observed in rheumatic fever were normal responses to hemolytic streptococcus infection or not. The data presented in this paper, in conjunction with findings referred to previously on other streptococcal infections, seem to indicate that the immune response of the rheumatic differ from the normal in that they are delayed. If this should prove to be true in the light of more extensive data on normal responses, then it must be assumed that the rheumatic subject who develops an attack handles the products of hemolytic streptococcus in a peculiar way. Such a concept harmonizes well with the prolonged antigenicity of this organism during rheumatic attacks as evidenced by the persistence of high antistreptolysin titre levels for months after infection. In addition to the apparent delay in the immune response of the rheumatic subject, there may also be a delay in the final elimination of hemolytic streptococcus products from the body. In conclusion, these observations suggest the hypothesis that the rheumatic state is characterized by an abnormal method of disposing of hemolytic streptococcus products. The mechanism whereby such an abnormal immune response may induce disease is unknown. Further information on the nature of this abnormality may make possible an experimental approach to the mechanism.

AUTHOR.

Norris, Robert F.: Primary Pulmonary Arteriosclerosis: Report of a Case With Marked Calcification of the Pulmonary Arteries. Bull. Johns Hopkins Hosp. **59**: 143, 1936.

A case of primary pulmonary arteriosclerosis with calcification of the pulmonary arteries is presented, and the evidence in favor of such a diagnosis is discussed.

It is suggested that some cases of emphysema may be the result rather than the cause of pulmonary vascular sclerosis.

Primary pulmonary arteriosclerosis is not a clinical and pathological entity but a syndrome.

AUTHOR.

Schmitt, H.: Experimental Observations on the Pathogenesis of Rheumatic Atherosclerosis. Virchows Arch. f. Path. Anat. **296**: 603, 1936.

Rheumatic atherosclerosis occurs in the aorta and coronary arteries only as a result of inflammatory degenerative processes. Animal experiments with serum injections convinced the author that the process is allergic with lipoid infiltration following cholesterol feeding. The lesions were localized here to the abdominal aorta. The involvement may be primarily medial or intimal.

L. N. K.

Pickering, G. W.: Observations on the Mechanism of Arterial Hypertension in Acute Nephritis. Clin. Sc. **2**: 363, 1936.

Raised arterial pressure in acute nephritis probably results from vasoconstriction because:

(a) In three cases the circulation time, as estimated by the decholin method, was essentially the same when the blood pressure was high and when it was normal.

(b) The blood viscosity was slightly decreased in three and slightly increased in one patient during the phase of hypertension.

In four out of six cases of acute nephritis estimations of blood flow showed that during the phase of hypertension no abnormal vasoconstriction was present in the hand from which vasomotor nervous tone had been completely removed.

Hypertension seems to be due to vasoconstriction which is of essentially different origin in acute and chronic nephritis; in the former it is probably of nervous origin in most cases; in the latter it is probably not.

AUTHOR.

Böger, A., and Wezler, K.: Action of Musculature on the Elasticity of the Living Arterial Wall: Its Relation to "Red" Hypertension. Klin. Wchnschr. **15**: 559, 1936.

The decreased distensibility accompanying blood pressure elevation produced by adrenalin (which the authors used to imitate change with age) occurs in the elastic aorta and the iliac arteries more markedly than in the brachial-radial arteries. Muscular contraction apparently makes the muscular arteries more distensible and so counteracts the action of the rising internal pressure. The increased distensibility acts as a compensatory mechanism to overcome the handicaps of the acute hypertension. The state of tone of these muscular arteries, thus, plays an important rôle in determining their distensibility. The methods of making these observations in man are described.

In patients with "red" hypertension observations indicate that this protective function of the smooth muscle is greatly disturbed. The pulse wave velocity was found to be greater in the muscular arm arteries in patients under fifty years of age with essential hypertension than in those of the same age without hypertension (even when the readings were corrected for the same internal pressure). In the case of the elastic arteries like the aorta no such difference in ratios for corrected pulse velocities could be made out between normal subjects and patients with hypertension.

L. N. K.

Geill, T., and Secher, K.: Studies Concerning the State of the Heart in Obesity: II. Obesity and Hypertension. Acta med. Scandinav. **87**: 454, 1936.

Studies on 31 patients were made. The electrocardiogram was abnormal in all; 6 had left axis shift. The electrocardiographic changes occurred in young individuals, none of whom had any nephritis. Hypertension and obesity form a serious combination in affecting the heart.

L. N. K.

Sappington, S. W., and Cook, Hunter S.: Radial Artery Changes in Comparison With Those of the Coronary and Other Arteries. Am. J. Med. Sc. **192**: 822, 1936.

The present study suggests: (1) That both age period changes and arteriosclerotic changes are maximal in the coronary arteries and minimal in the radial arteries and more or less intermediate in other vessels, such as the cerebral, splenic and renal arteries; (2) That atherosclerosis in the radial is such a rarity as to be negligible; and (3) That the anatomical condition of the radial artery has no bearing on visceral sclerosis.

Harkins, Henry N.: Mesenteric Vascular Occlusion of Arterial and of Venous Origin: Report of Nine Cases. Arch. Path. **22**: 637, 1936.

The literature on occlusion of mesenteric blood vessels is reviewed with special reference to the subject of secondary surgical shock. Except for very occasional citation, this aspect of the condition has received little clinical notice either in reports or treatment. On the other hand, the literature on experimental occlusions indicates that secondary surgical shock from loss of a blood plasmalike fluid into the peritoneal cavity or of blood into the wall or lumen of the intestine may be a major factor in death in these cases.

Nine cases of mesenteric vascular occlusion are reported. Most of these were observed before interest in the possible presence of shock was aroused and were not adequately investigated from this standpoint. One of the purposes of this paper is to enter a plea for more adequate study of such cases from the standpoint of shock.

A study of these cases indicates that arterial occlusion is more common than venous occlusion; that most of the patients are in the upper middle age group; that vomiting is frequent, and often bloody in the venous type; that abdominal distention with fluid is frequently present; that the white blood cell count is elevated; that the temperature is only moderately high; that pain is greater than the accompanying rigidity and tenderness would indicate; and that the condition may simulate mild intestinal obstruction due to malignant disease.

Accompanying the hemorrhagic infarction of the intestines are edema of the bowel wall and mesentery, bloody fluid in the lumen of the bowel with melena and bloody vomitus, and an exudate of blood-stained plasmalike fluid in the peritoneal cavity.

AUTHOR.

Adamek, G., and Friedländer, E.: Venography in Thrombophlebitis. Med. Klin. 32: 222, 1936.

Radiopaque material (perabrodil or tonobryl B) was injected in the superficial vein toward the foot and the leg quickly lowered. This permitted visualization of deep veins and permitted localization of the thrombosis in the iliac veins.

L. N. K.

Smirk, F. H.: Observations on the Causes of Edema in Congestive Heart Failure. Clin. Sc. 2: 317, 1936.

There is a fall in the colloid osmotic pressure of the plasma, and some protein passes through the blood vessels with the edema fluid. The colloid osmotic pressure of the protein of this edema fluid has varied between 1.5 and 7 cm. of water, and this acts in opposition to the colloid osmotic pressure of the plasma. Thus the effective colloid osmotic pressure is reduced, and as a result the reabsorption of fluid into the blood vessels is decreased.

At rest the venous pressure in the legs is approximately equal to the general venous pressure plus the pressure of a column of water extending vertically downward from the manubrium sterni to the situation where the venous pressure is measured. Active muscular movements of the legs diminish the venous pressure in the legs by 10 to 100 cm. of water. Thus the incapacity for exercise of patients with heart failure increases the average venous pressure in the legs, throughout the day, to much above the normal. The increase above the normal of the average venous pressure in the legs of heart failure subjects is produced mainly by their muscular inactivity and to a much smaller degree by the increase in general venous pressure. The increases in the general venous pressure in cases of congestive heart failure are not by themselves sufficiently great to cause edema. All factors increasing the local venous pressure, however, will increase the effective filtration pressure and thus will increase the rate of transudation of fluid out from blood vessels. Conversely the counter pressure of the edema fluid on the outside of the blood vessels, which is exercised as the edema accumulates, will decrease the rate of transudation of fluid.

The permeability of the blood vessels to water and to crystalloids is demonstrably increased in congestive heart failure and this augments the rate of flow of fluid from the blood vessels. The increase in the permeability of the blood vessels to water and to crystalloids may be such that with equal effective filtration pressures the rate of transudation of fluid in congestive heart failure is twice the normal. Increase in the permeability of the capillaries to water and crystalloids only influences the rate at which loss of fluid from the blood vessels occurs, and, despite such an increase in capillary permeability, fluid will leave the blood vessels only in situations where the effective capillary pressure exceeds the effective colloid osmotic pressure of the plasma.

The magnitudes of the various factors which combine to cause edema in congestive heart failure differ from case to case. Two of the important causes of such edema, namely the increase in the capillary permeability and the fall in the colloid osmotic pressure of the plasma, are also partly responsible for the edema in the nephrotic stage of glomerulonephritis.

AUTHOR.

Barsoum, G. S., and Smirk, F. H.: Observations on the Histamine-Yielding Substance in the Plasma and Red Cells of Normal Human Subjects and of Patients With Congestive Heart Failure. Clin. Sc. 2: 337, 1936.

A. The nature of the histamine-yielding substances in blood.

It was shown by Barsoum and Gaddum that when blood is extracted by the method described in their paper, a substance appears in the extract which has many properties in common with histamine. The evidence that this substance in the extracts is actually histamine appears to be strong and is further supported by our observation that the histamine-like activity of the extracts is destroyed by a preparation containing histaminase. This paper concerns the nature of the mother substance in blood which on extraction by Barsoum and Gaddum's method yields a histamine-like body. The following observations show that H.Y.S. (histamine-yielding substance) has biological properties which bear a striking resemblance to those of histamine and that H.Y.S. may be identical with histamine.

The histamine-yielding substance (H.Y.S.) in normal blood and blood from heart failure cases, as estimated by Barsoum and Gaddum's method, is destroyed by a preparation containing histaminase.

The H.Y.S. is present in human liver and injections of watery extracts of liver produce a fall of blood pressure in anesthetized dogs. The substance which produces this fall of blood pressure is mostly destroyed by a preparation containing histaminase.

Rabbits' cells contain a high concentration of H.Y.S., and laked rabbits' blood, when injected intravenously, causes a fall of blood pressure of the anesthetized dog, and when applied directly to the isolated guinea pig ileum causes it to contract. These histamine-like properties are destroyed by a preparation containing histaminase, and destruction is associated with a decrease in the concentration of H.Y.S., as estimated by Barsoum and Gaddum's method.

It is characteristic of histamine that the exposure of the isolated guinea pig's ileum to high concentrations of histamine desensitizes the ileum to a subsequent dose of histamine but does not desensitize it to other stimulants. It is found that the guinea pig ileum when desensitized to histamine is also desensitized to laked rabbits' blood, which blood fails to cause contraction of the desensitized ileum. Likewise the guinea pig ileum can be desensitized to histamine by the previous application of laked rabbits' blood. The laked rabbits' blood after treatment with a preparation containing histaminase loses its capacity to desensitize the guinea pigs' ileum to histamine and to laked rabbits' blood untreated with the preparation of histaminase.

Equal doses of histamine and of H.Y.S. (as estimated by Barsoum and Gaddum's method) cause equal contractions of the isolated guinea pig ileum and equal falls of blood pressure in anesthetized dogs.

B. The histamine-yielding substance in the blood of congestive heart failure cases.

It was found that in congestive heart failure cases there is an increase in the concentration of H.Y.S. in whole blood, which is due exclusively to the increased concentration of H.Y.S. in the red cells. H.Y.S., when confined within the red cells, fails, however, to produce its usual depressor action upon the blood pressure. Thus the absence of any measurable increase in H.Y.S. in the plasma of heart failure cases seems to explain fully the absence of physiological or symptomatic indications of the excess of histamine in the whole blood of these cases.

The concentrations of H.Y.S. in plasma and in plasma transudates such as edema fluids and pleural fluids are approximately equal. This suggests that the H.Y.S. found in the plasma in vitro is present also in vivo.

The concentration of H.Y.S. in plasma and edema fluid from congestive heart failure cases is within the normal limits. This suggests that the presence of an excess of H.Y.S. in whole blood does not explain the increased permeability of the capillary bed in congestive heart failure.

AUTHOR.

Barsoum, G. S., and Smirk, F. H.: Observations on the Increase in the Concentration of a Histamine-Like Substance in Human Venous Blood During a Period of Reactive Hyperemia. Clin. Sc. 2: 353, 1936.

During reactive hyperemia of the human arm, following a period of complete obstruction to the circulation, there appears in the venous blood an increase in the concentration of a substance which has the biological properties of histamine. It is thought that the liberation of this histamine-like substance during circulatory arrest accounts at least in part for the hyperemia.

Gollwitzer-Meier, Kl.: Observations on the Circulatory Action of Some Analeptics. Klin. Wchnschr. 15: 508, 1936.

It was observed that large doses of coramine can make the normal and insufficient heart in the heart-lung preparation beat more poorly and less efficiently in terms of energy cost. Large doses of cardiazol do not have this detrimental action. In small doses both drugs improve the insufficient heart. They have no action on the coronary blood vessels.

In the intact circulation these drugs increase the venous return to the heart which in turn increases minute-volume flow. The arterial blood pressure rises and hence the coronary flow increases. In cats they cause, by central vagus action, a slowing of the heart.

L. N. K.

Brückner, G.: The Venous Pulse Contour in Silicosis. Deutsches Arch. f. klin. Med. 178: 604, 1936.

It was found that evidence of congestion in the right heart following silicosis manifests itself in the venous pulse. These affect the diastolic waves.

L. N. K.

Kjaergaard, Hans: Roentgenkymography in Diseases of the Heart. Acta med. Scandinav. Supp. 78: 1936.

It is felt that kymography is the future method for x-ray examination of the heart and that it will rank with the other methods of examination as a valuable supplement to auscultation, sphygmomanometry and electrocardiography. But, however valuable the kymography, it must not be overestimated and made the sole basis for the diagnosis, prognosis and therapy—no more than the other methods of examination. The most important basis for the judgment of a cardiac patient is now, as well as before, the clinical observation of what Mackenzie called "the response to effort."

AUTHOR.

Faber, Borge, and Kjaergaard, Hans: Kymographic Studies on the Influence of Brief Muscular Work Upon the Heart Function. Acta med. Scandinav. 89: 537, 1936.

On comparison of the changes in kymographic demonstrations of the heart in young normal individuals before and after brief muscular work, the authors believe that

brief exerting work produces changes in the heart similar to those demonstrable after more protracted work. These changes are increase of the heart rate, increase in the power of the individual contractions associated with a rise of the blood pressure, a diminution of the heart both in systole and in diastole, besides increase in the amplitude of the movements of the different regions of the heart; presumably the last-mentioned condition is the cause of the increased beat volume.

AUTHOR.

Dahm, M., and Meese, J.: Mediastinal Movement in Aortic Aneurysm. Fortsch. a. d. Geb. d. Röntgenstrahlen **53**: 625, 1936.

The bronchial stenosis caused by aortic aneurysm is visible by x-ray, and the movements can be shown in the roentgenkymogram. Not all movements are due to bronchial stenosis. Anomalies of the diaphragm and pleural adhesions can also cause this phenomenon.

L. N. K.

Tilk, G. V.: The Relation of the Shadow of the Large Blood Vessels to the Depth of the Chest. Ztschr. f. Kreislaufforsch. **29**: 2, 1937.

This study is based on an analysis of twenty-five cases. No relation was found between the x-ray shadow of the great vessels of the heart and the depth of the chest.

L. N. K.

Heckmann, K.: Actinocardiography. Klin. Wchnschr. 15: 757, 1936.

The light intensity of the heart shadow cast on the fluorescent screen by the x-ray machine is recorded by means of a photoelectric cell. The current from the photoelectric cell is amplified and recorded with a mirror galvanometer on moving photosensitive paper. This gives a volume curve of the heart (or other organ). This method shows that the recently developed ionographs are not suitable for volume recording. The method which the author describes gives not only the changes in the intensity of the heart shadow, but also the changes in its size. For this reason displacements of the heart have no effect on the curve.

L. N. K.

Holzmann, M.: Social-Medical Needs for Cardiac Patients. München. med. Wchnschr. No. 20, 812, 1936.

The author points out that while good results often follow hospital care of cardiac patients, one-half the patients return one or more times for further hospital care. He believes, therefore, in the establishment of convalescent and training stations for cardiacs after their release from the hospital and in the better control of these patients after their discharge into an ordinary or restricted existence.

L. N. K.

Korns, Horace Marshall, and Feller, Alto E.: Treatment of Occlusive Arterial Disease of the Extremities by Passive Vascular Exercise: Report of Sixty-Eight Cases. Arch. Int. Med. **59**: 705, 1937.

Experience indicates, as does that of many other observers, that if collateral pathways are potentially adequate, passive vascular exercise helps to reestablish the circulation in an extremity which has been deprived of part of its blood supply by obliterative arterial disease.

AUTHOR.

Book Reviews

PASSIVE VASCULAR EXERCISES. By Louis G. Herrmann, A.B., M.D. 288 pages, 80 illustrations, and 4 color plates. Philadelphia, 1936, J. B. Lippincott Company.

This volume represents a timely presentation of the use of one of the most popular of the numerous mechanical devices which are so rapidly being produced in what might be termed as the machine age in medicine.

As the author points out in an instructive historical review, the principle of the use of pressure and suction together or separately in the treatment of vascular diseases is not a new one, having been in use more than 150 years, and in a form not dissimilar from the present in certain respects since 1798. The historical section seems unduly illustrated with modern apparatus including photographs of little significance such as those on pages 59, 63, and 68.

Certain contraindications to the use of the pressure suction apparatus have been noted, such as acute or subacute thrombophlebitis, obliteration of the arteriolar bed, acute infectious processes, and cellulitis. In addition, it is stated that no permanent benefit could be expected in conditions of high grade angiospasm of central origin. With these statements no one appears to differ.

On the other hand, it has been the experience of certain workers that the outstanding results claimed in this volume could not be duplicated with the same degree of success. Even the simple and fundamental observation regarding the elevation of surface temperature (p. 94) following the use of the apparatus has not, in the experience of the reviewer and others, been capable of constant reproduction. In fact, frequently the temperature of the skin has been lower after the treatment than before. This is in part, at least, responsible for the use of artificial hyperthermia as an important adjunct to the treatment. One might then question the relative merits of the two forms of treatment thus incorporated.

Although the reviewer agrees with the author in his belief that the clinical names of these diseases are of slight importance compared with an understanding of their pathological physiology, exception may be taken to the classification of the diseases as listed under the heading Primary Obliterative Arterial Diseases of Extremities (p. 126). Many of the conditions so listed are definitely secondary to external causes and should hardly be termed as primary, i.e., ligation of major artery, gunshot wounds, burns, etc.

Certain workers might question the occurrence of syphilitic thromboarteritis obliterans as a relatively common disease, as would be indicated by the author's series of six cases. The presence of a positive Wassermann test in a patient with arterial disease does not seem sufficient evidence in itself for the diagnosis but needs the further substantiation of the detection of the spirochetes in the walls of the vessels.

A useful chapter on the general management of arterial diseases is somewhat marred by the fact that it is practically confined to favorable reports of work with a number of substances presented in an uncritical manner. Negative and critical results have been published regarding certain of these substances and such data are at least as important in evaluating the true value of a given form of therapy.

The value of the pressure suction therapy is perhaps most widely accepted in the treatment of acute arterial emboli to the extremities. Yet even here the interpreta-

tion of results must be tempered by the fact that many of these cases clear up with the use of general heat, alcohol, etc., that the phenomena of apparent embolism may follow trauma and local phlebitis of an associated vein, which conditions clear up spontaneously, and lastly that a certain percentage of cases with embolism fail to respond even to this apparatus. These different aspects should be more critically evaluated.

In the treatment of frostbite Herrmann reports the good results which have been confirmed elsewhere.

The good results noted in cases of organic arterial disease complicated by infection, especially in diabetics, have not been duplicated, even with the addition of hyperthermia, in the experience of the reviewer and of other workers. In fact, in many such patients the infection appears to be aggravated.

Herrmann has found the machine to be of little value in the treatment of thromboangiitis obliterans, and in this we absolutely concur.

The problem with which workers in the field of diseases of the peripheral vessels are confronted appears to be not whether this and certain other machines will help to improve the circulation and restore these patients to health, but rather, whether the elaborate and expensive equipment will do this more satisfactorily than the *careful* use of the many simple measures which are available, and, if so, how much better? These questions are as yet unanswered in the minds of many careful observers. It must however be realized that our equipment of today in all probability does not represent the ultimate.

This volume may be regarded as a record of a clinical group which has had extensive experience with a rediscovered form of therapy. As such, it is of value for the inclusion of many new findings and as an aid to all others wishing to undertake this therapy.

ESSENTIALS OF ELECTROCARDIOGRAPHY. By Richard Ashman, Ph.D., Professor of Physiology, Louisiana State University Medical Center, and Director of the Heart Station Charity Hospital, and Edgar Hull, M.D., Assistant Professor of Medicine, Louisiana State University Medical Center. 212 pages, price $3.50, New York, 1937, The Macmillan Company.

This book is well printed and amply illustrated. It starts with a brief discussion of the instrument and a very good review of the physiology of the heart muscle. This is presented in a diagrammatic manner which is easy to comprehend, but, because it is diagrammatic, it gives the impression that many details are much more clearly understood than is actually the case. The illustrations throughout the book are accompanied by detailed interpretations of the records. These interpretations are conservative and should be very helpful to one learning to read the electrocardiogram.

One somewhat feels the absence of a presentation of the anatomical features upon which the spreading of the contraction wave must depend. Possibly, however, most of those who read this book may already have this knowledge in their minds.

The order of considering the various waves of the electrocardiogram is logical but the fact that normal and abnormal variations of the waves are considered in the same section leads one sometimes to a consideration of abnormal features in a record, which have not yet been described in their normal aspects. This might make it difficult for a beginner at the first reading of the book, but owing to the clearness and completeness of the descriptions, the second reading should lead to a good understanding of the subject.

The attempt to discuss special electrocardiographic features associated with different etiological types of heart disease leads to a certain amount of repetition.

It has a value to the beginner, however, in showing that electrocardiographic changes are due to myocardial lesions of certain pathological types rather than to the influence of any etiological factor.

The final section on cardiac arrhythmia is sufficiently complete and the illustrations are satisfactory.

THE FUNDAMENTALS OF ELECTROCARDIOGRAPHIC INTERPRETATION. By J. Bailey Carter, M.D., Clinical Instructor, Dept. of Medicine, Rush Medical College, Chicago, Ill. 326 pages, price $4.50, Springfield, Ill., 1937, Charles C. Thomas.

The printing and illustrations are good. The author makes a clear presentation of the origin of the waves of the electrocardiogram and shows many illustrations of its variations. Interpretations beneath these records would be helpful were it not that many of them overaccentuate the abnormality of certain features of the records. This is particularly true in regard to notching and slurring of the QRS group. Many times this is mentioned when very slight in degree and is often made the basis for a statement that myocardial damage is present when it seems likely that most electrocardiographers would disregard its presence. This is especially so in Figures 43, 44, 46 and in several others.

Figure 206, showing a curve commonly found in patients with hypertension, is said to "indicate a serious prognosis." This statement is not yet sufficiently established to be made in so unqualified a manner. Many other statements would not be generally agreed with, such as that "the S-T interval represents the period of electrical balance between cardiac apex and base"; also "all waves and intervals are best studied in Lead II." Pulsus trigeminus is illustrated by a record showing the recurrence of a group of three normal beats and a ventricular premature beat. There are so many statements throughout this book to which exception must be taken that the good features of the book are counteracted by the danger that the beginner will be misled.

THE COURSE OF THE ESOPHAGUS IN HEALTH AND IN DISEASE OF THE HEART AND GREAT VESSELS. By William Evans, M.D., F.R.C.P. Paper, 93 pages, London, 1936, His Majesty's Stationery Office.

The work described in this report was done by Doctor Evans at the London Hospital with the assistance of a grant from the Medical Research Council. The observations are confined to alterations of course and lumenal contour of the esophagus produced by adjacent normal or diseased organs. Abnormality arising in the lumen or wall of the esophagus itself is excluded from the scope of the brochure. Doctor Evans' report, which is profusely illustrated with roentgenograms and drawings, embodies his own studies of living persons and careful dissections of three cadavers, together with numerous citations from the literature. Among American observations cited are those of Rigler, Steel, and Mahaim. Impressions and deviations produced by the aortic arch, left bronchus, left auricle, descending aorta, and enlarged lymph nodes are described in detail. The booklet is comprehensive in its covering of the subject and is valuable to the radiological diagnostician.

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An asterisk (*) indicates that the reference is an abstract and not an original article.

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